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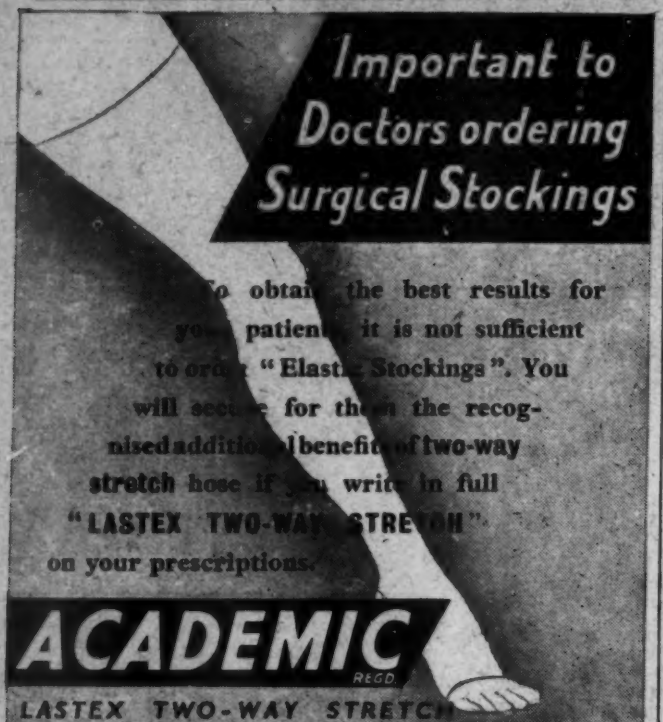

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BRITISH MEDICAL JOURNAL

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THE PHYSIOLOGY AND RELIEF OF TRAUMATIC ARTERIAL SPASM*

BY

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When these lectures were founded by Edward Arris in 1646 the lecturers were called the "Readers of the Muscular Lecture." Such a title would be appropriate to-day because the studies to be described deal largely with muscle. It is not, however, the striped muscles described in the old "Public Anatomies" but the smooth muscle of blood vessels which will be considered here.

The clinical aspects of traumatic arterial spasm must be briefly discussed before considering the physiology of its production and relief. The larger vessels of the limbs such as the brachial or femoral arteries are those usually affected, and the spasm follows injury near by, often a fracture, dislocation, or gunshot wound. Sometimes the cause may be dissection of an artery during a surgical operation such as arteriography or vein ligation. A length of vessel may remain in spasm for hours or even days, and ischaemic contracture of muscle or gangrene of the limb may result. This contractile power of major arteries has been known for many years. Hunter, who with Pott gave the first Arris and Gale lectures under the Company of Surgeons, was aware of it. He described many instances in man and animals, and knew that it was part of the natural mechanism for suppressing bleeding (Hunter's Works, 1835). When, however, an artery is injured without being opened this protective mechanism is unnecessary because there is no bleeding to stop, and harmful because the circulation to the part is arrested. More recently the clinical side of the problem has been well described by Cohen (1940) and Griffiths (1940) in Hunterian Lectures, but until the work of Barnes and Trueta in 1942 there had been few investigations of the cause or cure of arterial spasm under experimental conditions. This is unfortunate, because the difficulty of obtaining standard conditions has always made it hard to judge the effects of treatment in clinical practice. The artery affected, the type of injury, and the time that has elapsed before the treatment starts may all vary from one patient to another. The present studies were chiefly made in the laboratory. They will be considered in two parts: (1) the causes of arterial spasm or other alterations in the size of large arteries; and (2) the cure of arterial spasm.

Causes of Spasm or Other Alterations in Size of Large Arteries

The concept of a nervous reflex arc has been widely held. Barnes and Trueta (1942) and Trueta and his colleagues (1947) described experiments in rabbits in which a tourniquet applied to the thigh for several hours produced shrinking of the femoral artery on the other side. These findings were taken as the basis for studies made at Harvard in 1948. The details of some of these earlier experiments have already been published (Kinmonth, Simeone, and Perlow, 1949), so that it will now only be necessary to outline them in order to understand what follows. The tourniquet experiments of Trueta and his co-workers were repeated, using a technique which allowed continuous observation and measurement of the arterial diameter. The arterial tree on the side opposite to the tourniquet shrank in the way in which they had described. This shrinking occurred gradually and coincided with a slow fall in blood pressure in a way suggesting a close relation between the two. Tourniquet experiments were then done on rabbits in which bilateral lumbar sympathectomy or denervation of the hind limb had been performed. The same shrinking of the arterial tree on the opposite side took place except in animals in which the blood pressure remained level. This suggested that a gradual fall in blood pressure might cause a parallel shrinking of the femoral artery independently of the presence of intact nerve pathways.

The next step was to see whether alterations in the blood pressure due to other causes might change the arterial diameter. Different methods of altering the blood pressure were used and the effects on the upper third of the femoral artery recorded. The results are shown in Table I. They refer to findings in the rabbit except in the case of "priscol," where these experiments were done on the cat. Priscol (tolazoline hydrochloride) is a benzyl-imidazoline compound which dilates the small vessels of the peripheral circulation. It has a depressor effect in the cat, and this makes the femoral artery shrink.

TABLE I.—*Effect of Blood-pressure Changes on the Femoral Artery*

	Blood Pressure	Arterial Diameter
Open ether	↓	↓
Pentobarbitone sodium (i.v.)		
"Shock" due to tourniquets, haemorrhage, etc.	↓	↓
Priscol (i.v.) (cat)		
Afferent nerve stimulation	↑	↑
Adrenaline (i.v.)		
Tracheal obstruction	↑	↑

The arterial diameter follows the changes in blood pressure whatever the effect of any particular agent may

*Based upon an Arris and Gale Lecture given at the Royal College of Surgeons on May 29, 1951.

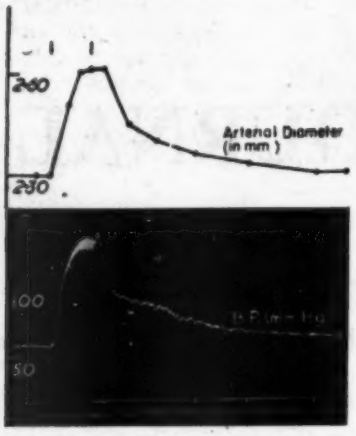

FIG. 1.—Effect of tracheal obstruction on the systemic blood pressure and femoral artery of the rabbit. Anaesthesia with urethane. Arterial diameter measured just below inguinal ligament. Trachea obstructed from second to fifth signals. Time signal (lowest record), 10 seconds.

be upon the peripheral part of the arterial tree. Fig. 1 shows how the femoral arterial diameter changes with the rise in systemic blood pressure when the trachea is temporarily closed.

It follows that the blood pressure should always be recorded in experiments on arterial spasm, otherwise changes in arterial size due to alterations in blood pressure may be falsely attributed to efforts to produce or to relieve spasm.

The concept of a nervous reflex arc was further examined by tests on its possible efferent components. The femoral artery was chosen for detailed study in the rabbit, and tests were made in three ways. First, the artery was stimulated directly with a faradic current. This had no effect on the upper third near the inguinal ligament, but further down marked contraction resulted. Secondly, the lumbar sympathetic chain was stimulated electrically. This had no effect upon the upper third of the femoral artery although shrinking of the paw recorded by a plethysmograph showed that the stimulus was effective. Lumbar sympathetic stimulation provoked a marked contraction of the more distal part of the femoral artery. The third method of testing for the efferent component of a reflex arc was to give an intravenous injection of adrenaline and record the change in the femoral arterial diameter. Fig. 2 shows the effect of an intravenous injection of adrenaline on the blood pressure and the diameters of the upper and lower parts of the femoral artery observed simultaneously with two microscopes. The lower part of the femoral artery was seen to contract, but the upper part actually dilated in phase with the rise in blood pressure. Had there been adrenergic sympathetic motor-nerve endings in the upper one-third of the artery the adrenaline would have been expected to have acted upon them to cause contraction.

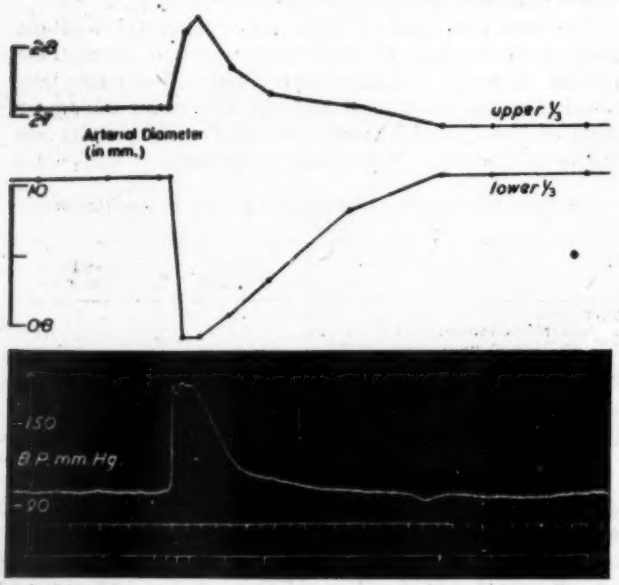

FIG. 2.—Effect of adrenaline on the systemic blood pressure of a rabbit and on its femoral artery measured simultaneously 3 mm. and 80 mm. below the inguinal ligament. Urethane anaesthesia. Injection of 1 ml. of 1 in 50,000 adrenaline intravenously at fifth signal (lowest record). Time signal, 30 seconds.

These observations were repeated many times with consistent results and recorded in detail elsewhere (Kinmonth and Simeone, 1952). They revealed no evidence of vasoconstrictor nerve supply to the upper third of the femoral artery, and yet this part of the vessel may be readily put into spasm by mechanical trauma, and on microscopical examination is found to contain much smooth muscle in its wall.

A similar state exists in man, although it has not yet been possible to determine in detail the level at which the motor-nerve supply becomes evident. Fig. 3 shows how electric stimulation of the dorsalis pedis artery of a patient during the course of a surgical operation produced a definite contraction.

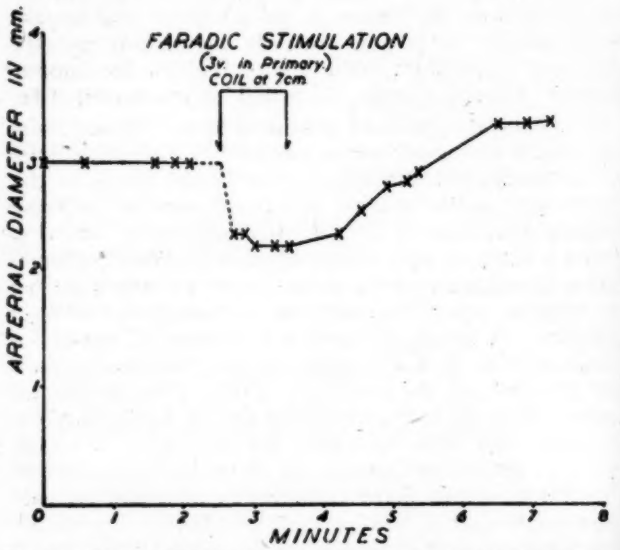

FIG. 3.—Contraction of a healthy small artery (the dorsalis pedis) in response to direct electric stimulation in a woman aged 27.

Stimulation of larger vessels such as the common femoral artery (Fig. 4) produced no contraction. This particular common femoral exhibited partial traumatic spasm when a needle was introduced later for arteriography.

Dr. F. A. Simeone has tried the effect of a variety of direct electric stimuli on large arteries during the course of surgical operations, but always without causing contraction. I have found the same, and yet these arteries will go into spasm if subjected to mechanical trauma.

Arterial spasm may be produced in the experimental animal by applying mechanical trauma to the artery in different ways. Pinching, longitudinal traction, handling with forceps, or rubbing with gauze may cause it. Sometimes additional trauma may produce a localized fusiform dilatation with spasm at each end similar to that described by Grant (1930) in the main artery of the rabbit's ear. The actual irritability of the vessels and their response to trauma vary. It is difficult to produce spasm a second time after relaxation has occurred, and sometimes an animal is found in which it cannot be produced at all. The causes of these variations in irritability are not clear, and are being studied further.

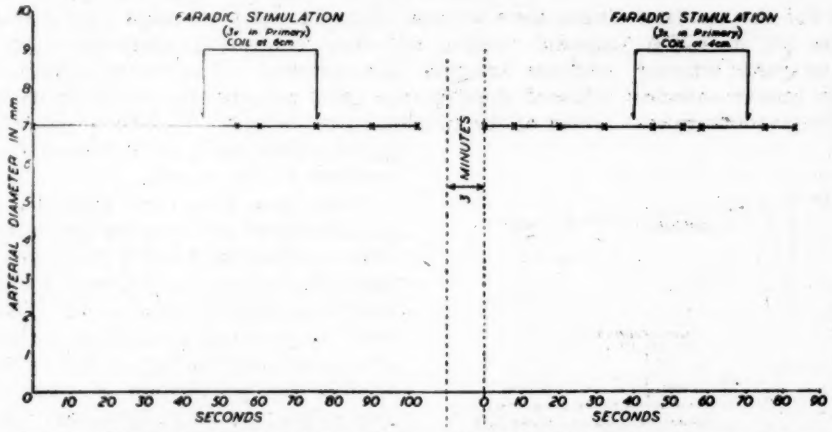

FIG. 4.—Direct electric stimulation of large arteries, in this case the common femoral of a woman aged 42, causes no contraction, although mechanical stimuli may do so.

That an intact sympathetic nerve supply was unnecessary for the maintenance of arterial spasm was shown by experiments in rabbits in which spasm was produced by deliberate periarterial stripping of the vessel. The arterial wall was cleanly stripped of its adventitia and possible nerve supply, and yet the spasm lasted for one to two hours. In man, also, local arterial spasm can persist for long periods after the sympathetic nerve supply has been removed from vessels by the operation of periarterial stripping.

It was accepted as a working hypothesis that traumatic spasm is due to mechanical stimulation of the vessel wall resulting in a sustained contraction of smooth muscle in the maintenance of which nervous factors do not play a demonstrable part. With this conclusion in mind, methods of relieving traumatic spasm were considered.

Methods of Relieving Arterial Spasm

At least a dozen different methods of relieving arterial spasm have been tried in clinical practice. They have included the intravenous injection of drugs and simple exploration as well as more drastic procedures like periarterial stripping or arteriectomy, and success has been claimed at times for almost all of them, even the most unlikely. The probable reason is that arterial spasm lasts for a variable time after the injury, and spontaneous relaxation may coincide with treatment.

In the laboratory, controlled experiments under standard conditions are possible and provide a more reliable test of the success or failure of therapeutic measures. Most of our experiments on the relief of traumatic spasm have been done on rabbits anaesthetized with urethane or "dial." A continuous record of the systemic blood pressure has been kept throughout with a carotid cannula and mercury manometer to prevent confusion due to possible changes in arterial diameter caused by alterations in blood pressure. The arterial diameter was measured by direct observation with dissecting microscopes fitted with micrometers. The upper third of the femoral artery just below the inguinal ligament was chosen for particular study, and this was put in spasm by deliberately rough dissection and then covered by normal saline solution to prevent drying. The vessel on the opposite limb was dealt with in the same way, and so far as possible at the same time, to provide a control. A series of animals were observed in this way to see how long the untreated spastic arteries took to relax. Fig. 5 is a typical example of the slow and gradual natural relaxation of the vessels, which was similar on the two sides. The rate of relaxation slowed down after two hours as the animal's condition deteriorated and the blood pressure fell.

A number of drugs were applied to arteries which had been put into spasm in the way described to see if they would relax them. The chief drugs chosen were known to have a direct action on smooth muscles, because the preliminary work had suggested that smooth-muscle contraction was the important factor in the spasm rather than nervous activity. Direct application was chosen because it was considered that substances circulating in the blood would have little chance of reaching the muscle in the arterial wall. Under clinical and experimental conditions the lumen of the spastic vessel is often totally closed and the vasa vasorum damaged by the injury which caused the spasm. Each drug was tested several times in different animals, and the results shown in the figures are typical examples.

The first substance to be used was papaverine, and Fig. 6 shows the result of applying a 2.5% solution of the sulphate to vessels which had been put in spasm in the usual way. Intravenous injection of papaverine was without effect on the spastic vessels, nor did it have effect on any of the numerous occasions on which it was tried in other animals—a finding in agreement with results in man (Learmonth, 1950, personal communication). The drug relaxed the vessels rapidly when applied direct to them, and they remained relaxed after it was replaced by saline. There was no rise in blood

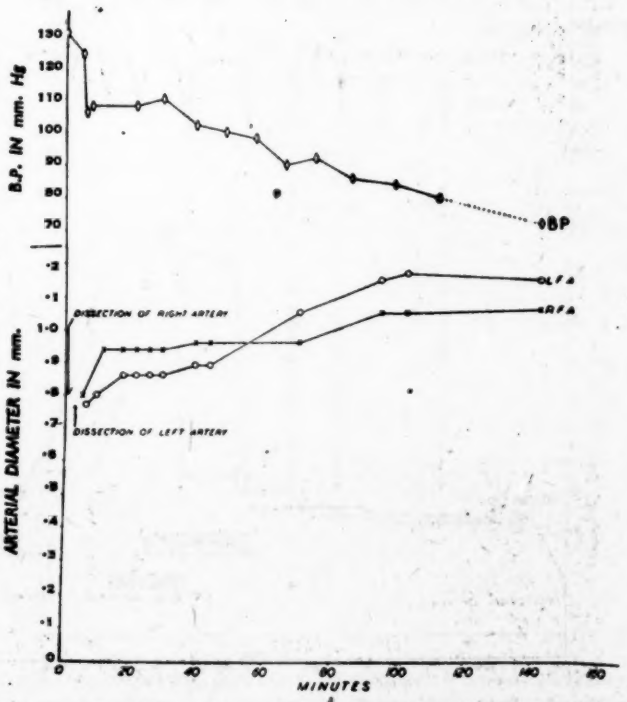

FIG. 5.—Example of the gradual and symmetrical way in which natural relaxation of traumatic spasm occurs in the femoral artery of a rabbit over a period of about two hours. Urethane anaesthesia.

pressure which could have accounted for the changes. In other animals more dilute solutions, 1% or 1.25%, were also effective when applied direct to spastic arteries.

The effect of caffeine, which is another smooth-muscle-relaxing agent, is shown in Fig. 7. Intravenous injections were without effect. Local application dilated the spastic vessels, but they contracted again after the caffeine solution was removed. The blood pressure showed some abrupt falls, perhaps due to the irritant effect of the caffeine citrate solution, but there were no peaks which could have caused the swelling of the vessels.

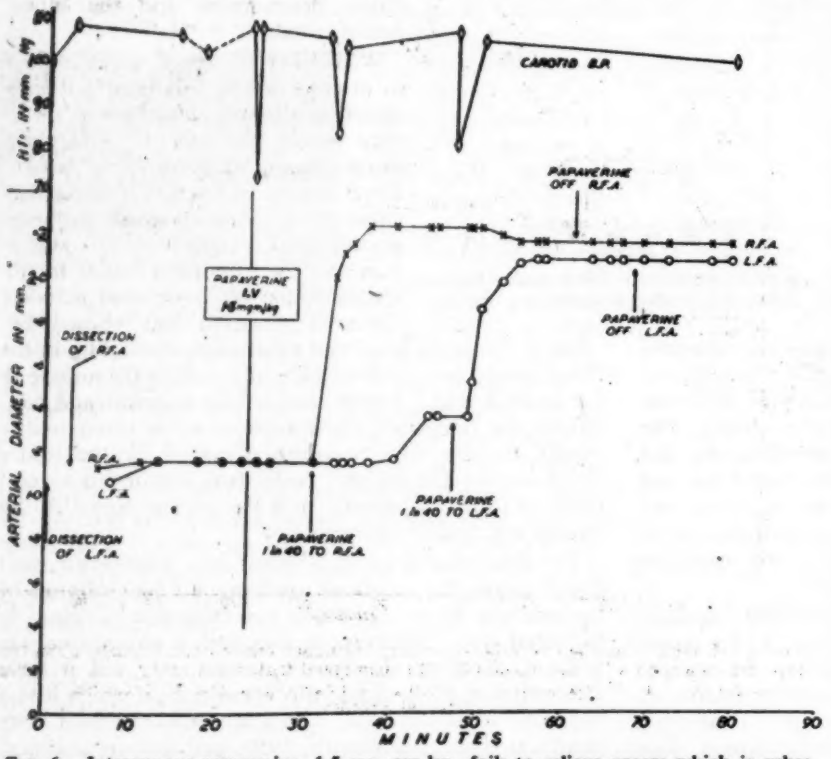

FIG. 6.—Intravenous papaverine, 1.5 mg. per kg., fails to relieve spasm which is subsequently relaxed by direct application of a 2.5% solution of the drug. The vessels remain dilated when the drug is removed. Arteries measured 11 mm. below inguinal ligaments. Rabbits anaesthetized with urethane

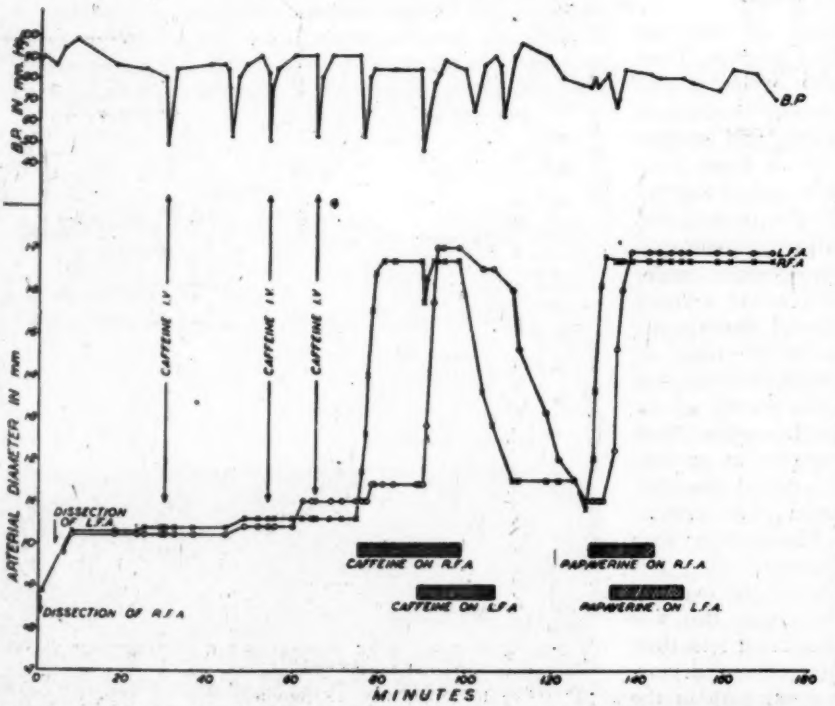

FIG. 7.—Rabbit anaesthetized with urethane. Spastic vessels unaffected by intravenous injections of caffeine citrate, 1.5 mg. per kg. Relaxation produced by direct application of 1% caffeine citrate retrogresses when this is replaced by saline. Permanent relaxation by 1% papaverine sulphate. Arteries measured 6 mm. below inguinal ligaments.

There have been some clinical reports of relief of spasm by irrigation with warm saline. Fig. 8 shows how repeated irrigation of the wound and spastic artery with saline at 50° C. at intervals produced gradual relaxation over a period of an hour. At the end of this time application of papaverine solution to the control artery on the other side caused a greater relaxation in a few minutes.

The relaxing effect of procaine on arterial spasm is shown in Fig. 9. In this animal there was no contraction of the vessels after the procaine was removed, but in others shrinking was observed. The permanence of the effect of procaine varies.

It was suggested to me by Dr. N. E. Freeman (1949, personal communication) that local application of heparin might be of value in relaxing spasm, as it is considered to have some dilating effects on small vessels as well as its effect on blood coagulation. That this might be so was also suggested by the fact that protamine sulphate, an antagonist of heparin, is known to contract arterioles and had been found in some of our experiments to produce a partial contraction of large arteries. A solution of heparin containing 1,000 units per ml. was therefore applied to the spastic femoral artery of a rabbit, but was found to have no effect upon the diameter. Subsequent application of papaverine produced prompt relaxation. In other animals, when its haemorrhagic effect did not obscure vision, heparin also failed to relieve arterial spasm.

Priscol, which relaxes small vessels, was also found to relax large arteries, as Fig. 10 shows, but the artery contracted again after the drug was removed. Similar results were obtained in other animals. Intravenous injections were without effect.

Another drug which was tried was benzodioxane. This is known for its so-called sympatholytic effects and its use in the diagnosis of phaeochromocytoma. It produced only partial relaxation, which could be completed by replacing the benzodioxane with papaverine. Inhalations of amyl nitrite were also tried. They produced falls in systemic blood pressure, but did not affect the spastic arteries.

Papaverine was the only drug of all those tried which consistently produced relaxation which did not retrogress if the drug was removed. It was used altogether on 31 spastic arteries, all of which it effectively dilated. Procaine and caffeine were the next most successful drugs.

Effect of Papaverine on Wound-healing

The effects of papaverine on living tissues were studied in rabbits before using it in human wounds. The femoral vessels and nerve were exposed, the artery was put in spasm by rough dissection, and the wound was filled with 2.5% papaverine solution. After fifteen minutes the wound was closed, leaving some of the solution inside. A similar operation was done on the opposite side, using saline. The two wounds healed equally, and histological examination, when the animals were killed at intervals of one to eight weeks, showed no difference between the tissues on the two sides. The papaverine solution sometimes turned blood clot in the wound to a brown colour, but this does not appear to have been harmful.

Clinical Application

The results of the many different forms of treatment which have been tried for arterial spasm are reviewed in Table II. The results of conservative operations, such as simple exploration and perhaps bathing the vessel with warm saline or serum, are compared with those of operations in which periarterial stripping or arteriectomy was performed. The cases in which gangrene or muscle contracture followed are classed as failures. These are the results of 59 cases published by various authors in which the diagnosis of traumatic arterial spasm was definite, and in which full details of the end-results were given.

The brachial and femoral were the arteries most often affected. There were most failures in the group in which stripping or arterial excision was done. This difference was particularly marked in the case of the brachial artery. The popliteal artery maintained its sinister reputation, with gangrene in three cases out of seven, even though treated by conservative operation.

Clinical and laboratory experience suggests the following scheme of management:

1. Early exploration of the injured vessel must be performed. It will then

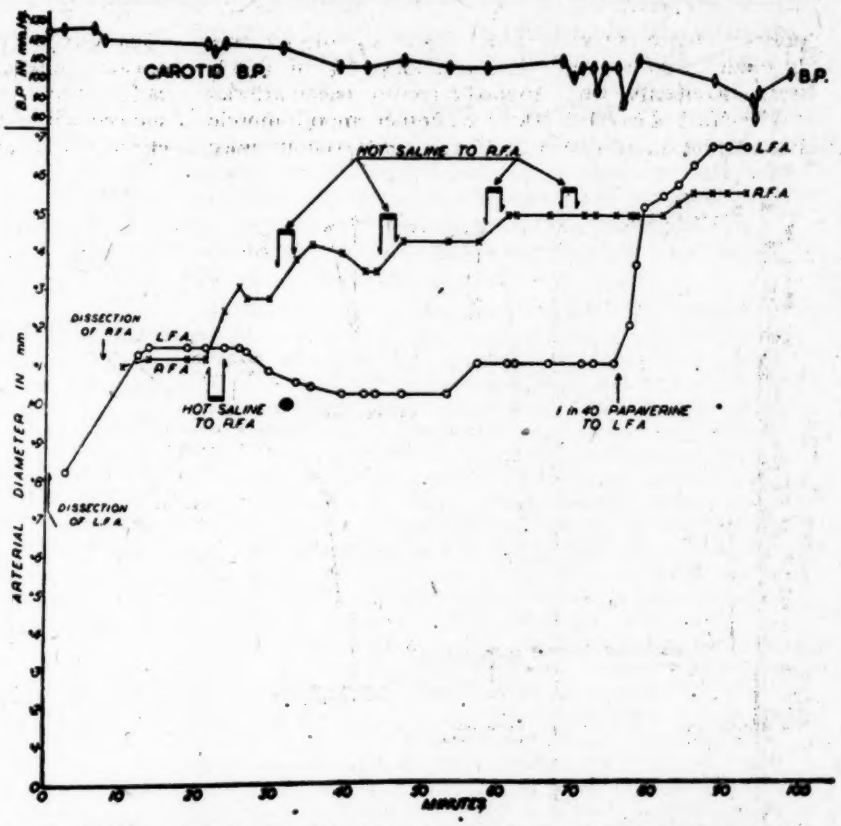

FIG. 8.—Rabbit anaesthetized with urethane. Gradual relaxation of spastic artery by repeated irrigation with hot saline (50° C.), compared with rapid and greater relaxation produced by 1 in 40 papaverine solution. Diameters measured in proximal third of femoral arteries.

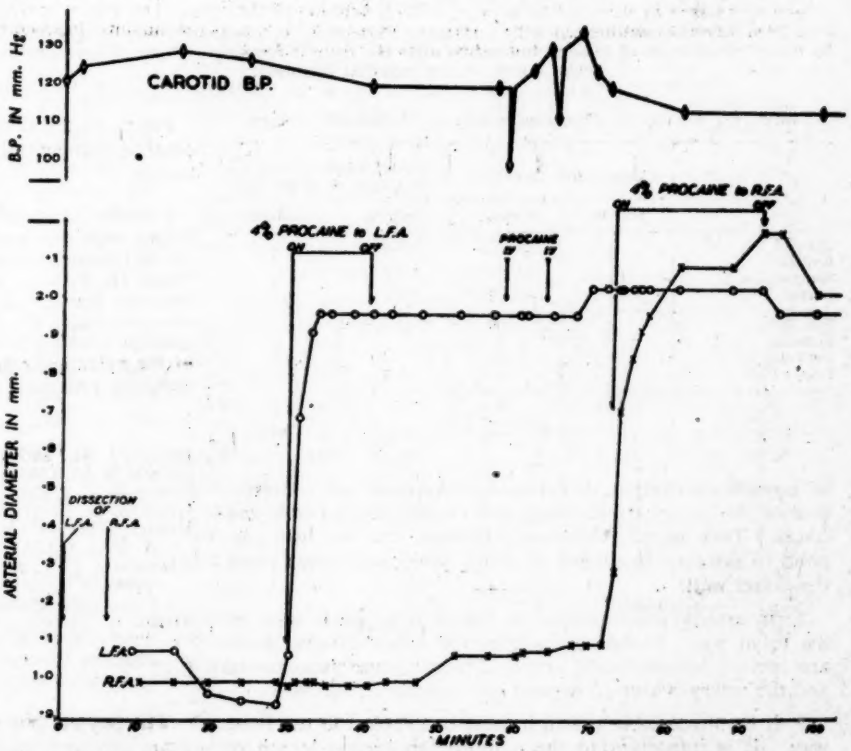

FIG. 9.—Rabbit anaesthetized with urethane. Direct application of 4% procaine solution dilates the left femoral artery, which does not constrict when the drug is washed off with saline. Intravenous procaine, 3 mg. per kg. and 6 mg. per kg., does not affect the right femoral artery, which is subsequently dilated by direct application of the drug. Diameters measured 1 mm. below inguinal ligaments.

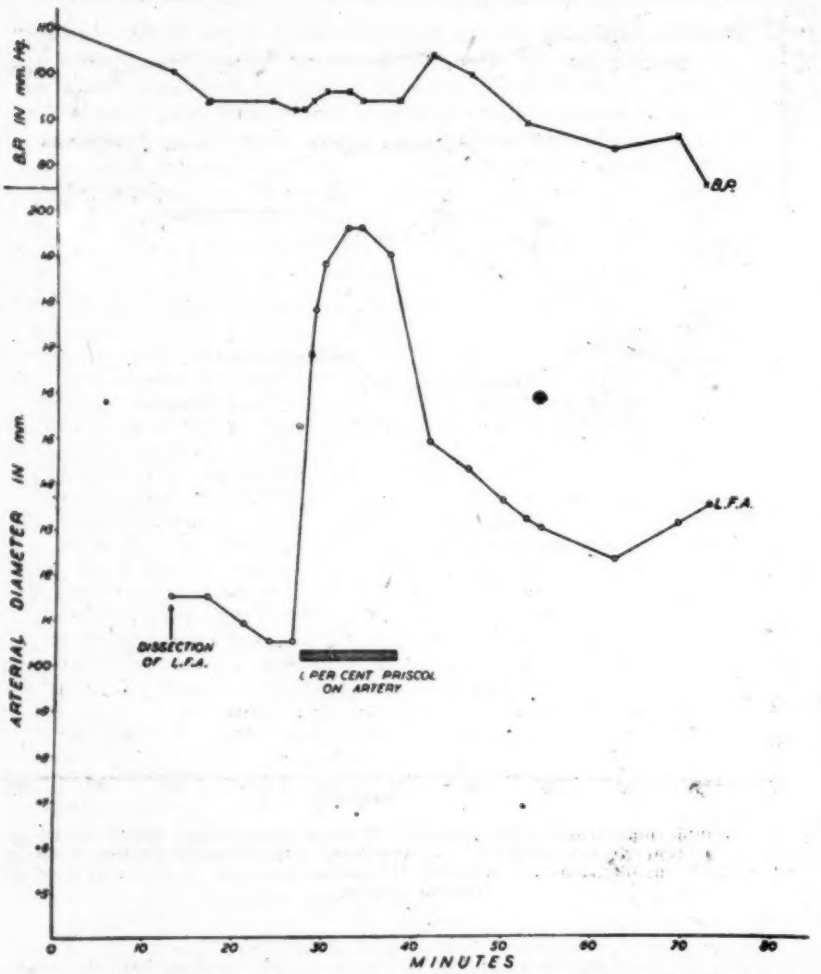

FIG. 10.—Rabbit anaesthetized with urethane. Spasm in left femoral artery is relieved by direct application of priscol, but recurs after the drug is removed. Point of measurement 7 mm. below inguinal ligament.

TABLE II.—*Results in Published Cases of Traumatic Spasm*

	Conservative Operation		Active Intervention (Stripping or Resection)	
	Success	Failure	Success	Failure
Carotid	1	—	—	—
Axillary	2	—	2	—
Brachial	12	—	6	8
Radial	4	—	1	—
Ext. iliac	2	—	—	—
Femoral ..	7	1	2	1
Popliteal	4	3	—	1
Post. tibial ..	—	—	2	—
	32	4	13	10

be possible to distinguish between true spasm and compression of the artery by bleeding and swelling under skin and fascia. They require different treatment. Neither will respond to systemic injections of drugs which will never reach the vessel wall.

2. If arterial compression is found it is dealt with in the usual way; blood clot is removed and skin and fascia are incised longitudinally until all constriction is removed and the artery is seen to expand and pulsate satisfactorily.

3. If the artery is in spasm it must be exposed in the same way. It is important to see a normal pulsating length of vessel above the spastic segment. If this is not done quite a short length of spasm remaining at the proximal end may prevent relaxed vessel below from filling with blood or dilating.

4. The artery is covered by a warm 2.5% solution of papaverine sulphate and left for a few minutes.

5. Should relaxation not occur within 10 to 15 minutes the wound is loosely closed, leaving a fine polythene tube down to the vessel for instillation of 1% papaverine at intervals until the circulation is restored.

6. It is important to treat shock and to restore a normal blood pressure on general grounds, and because spastic vessels will not dilate if the blood pressure is low.

This regime has been tried in two patients with arterial spasm occurring during operation. In both cases papaverine caused prompt relaxation.

Summary

Arterial contraction due to a supposed nervous reflex arc was explained by shrinkage due to falling systemic blood pressure. The diameter of large arteries changed with alterations in blood pressure produced by different means. Attempts to produce contraction of large arteries by electric stimulation of the efferent components of possible reflex arcs were unsuccessful.

Direct mechanical trauma applied to the vessel wall in various ways produced lasting spasm which could not be relieved by sympathectomy.

Attempts to relieve established traumatic spasm were therefore directed at paralysing smooth muscle itself rather than sympathetic nerves.

Smooth-muscle-relaxing drugs were successful in relaxing spasm when applied direct to the vessel. Intravenous injections were ineffective.

Papaverine was the most consistently successful in producing permanent relaxation. It was not injurious to living tissues.

I gladly acknowledge my debt to many people who have helped with this work: Dr. F. A. Simeone, with whom much of the fundamental part of the work was done at Harvard; Professor G. Perkins, at St. Thomas's, and Professor Sir James Paterson Ross, at St. Bartholomew's, in whose departments it was continued; Dr. G. Cunningham for his help with the microscopical histology; Mr. G. J. Hadfield, who helped with many of the operations; and Mr. F. Scholefield and Miss D. Gay for technical assistance.

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The Society for the Study of Fertility was founded three years ago with the intention of having a yearly congress for the reading of papers and free discussion of problems of fertility and infertility, not only in the human subject but in livestock and laboratory animals. The secretary is Dr. G. I. M. Swyer, University College Hospital, W.C.1.

A SIMPLE STANDARD EXERCISE TEST AND ITS USE FOR MEASURING EXERTION DYSPNOEA

BY

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With the assistance of A. V. LAMBERT

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In the management and study of patients who have their exercise capacity reduced by heart or lung disease some way of estimating the degree of breathlessness on exertion is often required. Only a rough estimate can be got from the patients' descriptions of their symptoms, which, although helpful in diagnosis, are inadequate for many purposes. An objective and more precise estimate is needed for a reliable judgment of the effects of treatment or for comparing one method of treatment with another, for assessing the patient's capacity for physical work during rehabilitation, for awarding compensation in industrial pulmonary disease, and for many types of survey investigation.

For these purposes various exercise-tolerance tests have been devised. A type of test which is simple, and commonly used, is to get the patient to step up and down from a stool or chair and, at the end of a period of exercise, to assess his response subjectively in terms of "breathlessness," or objectively by counting the respiratory and pulse rates. This sort of test has been criticized by a number of workers (Brittingham and White, 1922; Wahlund, 1948; Renner, 1951). There are two main objections to it as it is usually done:

1. The amount of exercise is not measured. It depends on the rate and time of stepping and on the height of the stool or chair, and also varies individually with the weight of the patient.

2. The ventilatory cost of the exercise is not measured. This cannot be measured by counting the respiratory rate, because the depth of breathing may not remain constant, while the recovery pulse is variable even in normal subjects and is not well related to ventilation (Cotton *et al.*, 1916; Mann, 1918; Reisinger, 1938; Belayew, 1948; N. P. V. Lundgren, 1951, personal communication), although some observers contend that the pulse rate gives useful information concerning the state of the circulation (Meakins and Gunson, 1916; Master and Oppenheimer, 1929).

A known amount of exercise can be given by a bicycle ergometer or a treadmill, but these machines are usually impracticable for clinical use owing to their complexity and immobility. Thus various modifications of the simple step-test have been suggested in attempts to make it objective and precise. Some of these, in which the subject's maximum effort is sought (Lundgren, 1949; Behnke, 1942) may be useful as efficiency tests in fit subjects but are too distressing for ill patients, while others (Nylin, 1933, 1936; Master, 1935), although they are submaximal tests and are designed to give quantitative results, have other drawbacks. Nylin's test requires a special stairway, and, although Master's test is simple, the results merely show whether a patient's exercise tolerance is "within average figures," the exact response being obtainable only by trial and error in repeat testing. Neither of these tests measures breathlessness.

In this paper, modifications to the step-test are described which allow it to be used for giving a standardized and known amount of exercise without appreciably impairing its simplicity. The response to it is measured in terms appropriate for the quantitative expression of breathlessness.

Principles of the Test

The exercise is standardized by arranging that every patient does the same amount of mechanical work with approximately the same efficiency. The ventilatory cost of the work is found by measuring the volume of air exhaled per minute for an appropriate time before, during, and after the exercise.

In arranging that each subject does a standard amount of exercise regardless of his weight the test resembles that of exercise with a bicycle ergometer. It differs from a step-test used by Baldwin, Cournand, and Richards (1948) in which the exercise is standard only "in that each subject performs a standard number of steps within one minute of time." It may be asked: Why use standard exercise for all patients when they vary in weight and have to carry that weight about? The answer depends upon what is required of an exercise test. If only a specific function such as a subject's ability to go up steps or to walk at a given rate is to be assessed, then clearly a direct test of this function is to be preferred to a standard test. Standard exercise is useful as a general test in that it is not specific to any particular task. Further, standard exercise is preferable for the assessment of change in ventilatory efficiency over a period of time—for example, in assessing the effects of treating heart failure, or when reassessing a patient for compensation, etc.—otherwise any change observed may merely be a reflection of a difference in the patient's weight. Lastly, if in a group of subjects one wants to know whether variations in their ventilation may be due to disturbed cardiopulmonary function a standardized test must be used; or, again, the variations may simply reflect differences in their weights.

Apparatus and Method

Standardizing the Exercise.—Since the external mechanical work performed in a step-test is a product of the patient's weight and the height and rate of stepping, it is evident that altering either the height or the rate of stepping can compensate for differences in weight between one patient and another and so keep the amount of work constant. However, the range of variation in weight that is commonly encountered is such that if stepping rate only were altered the lightest of subjects would have to step so quickly and the heaviest so slowly that the comparison between them would not be fair, since their physiological efficiency would not be comparable. Similarly, unfair comparisons might be made if only the height of step were changed. But if both height and rate

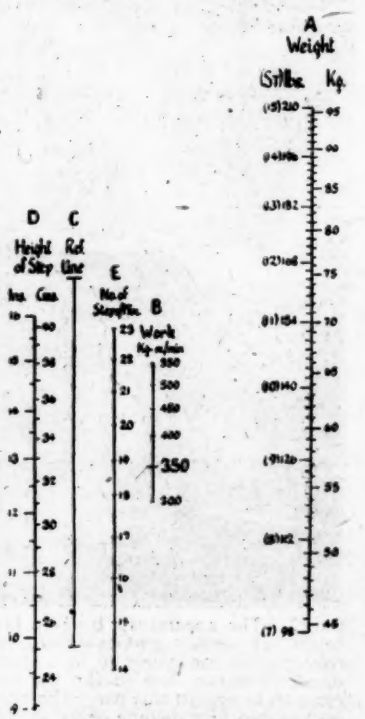

FIG. 1.—Nomogram for determining appropriate combinations of height and rate of stepping so that all subjects do the same amount of work in the step-test independent of their weight.

are altered to compensate for weight variations, large adjustments of either can be avoided. The appropriate height and rate of stepping are quickly found without calculation by using the nomogram reproduced in Fig. 1.*

The nomogram is used by placing a ruler on scale A at a point corresponding to the weight of the subject, and the ruler is then adjusted so that it passes through the amount of work chosen on scale B. The place where it intersects the reference line C is marked. The ruler is then laid across the scales D and E in any position, provided that its edge passes through the point marked on line C. The readings thus obtained from D and E will give a combination of height and rate of stepping which will ensure that the subject performs the chosen amount of work.

In preparing the nomogram scale E was limited so that its extremes were within the flat-topped part of the well-known curves relating rate of muscular contraction and physiological efficiency (Lupton, 1923; Garry and Wishart, 1931). Scale D was limited so as to avoid large changes in knee-angle and hence in available leg-thrust (Hugh-Jones, 1947). If the ruler is kept reasonably horizontal through the point found on scale C, any changes in physiological efficiency between one subject and another due to change in height and rate of stepping will be minimized. It has been found experimentally that, even when the extremes of the height and rate lines are used, efficiency is not appreciably affected (see the results of the appraisal of the test below).

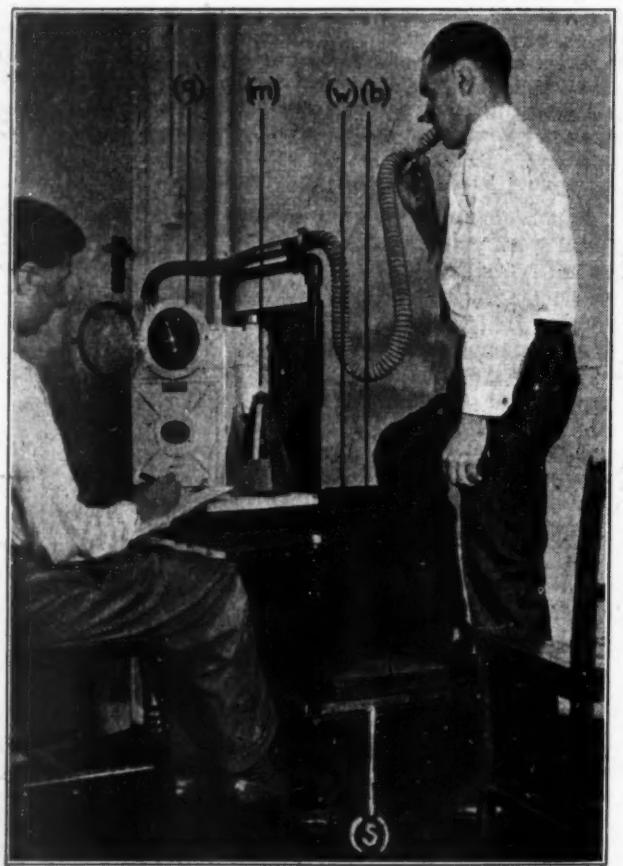

FIG. 2.—The apparatus. b=¼-in. (1.25 cm.) boards for altering height of step. g=Gas-meter. m=Metronome. s=Stand. (Note: It is convenient to fit a sloping bar of wood (w) to the stand, as shown, and to slot the boards (b) in the appropriate place to fit against this bar. The boards can then only be placed on the step in a definite order so that each can be marked with the height of step formed when it is at the top of the pile.)

*Full-size photographic copies of the nomogram (10 by 8 in.—25 by 20 cm.) are available on application to the Director, M.R.C. Pneumoconiosis Research Unit, Llandough Hospital, near Cardiff. Price 2s.

Equipment.—Three simple pieces of equipment are used for the test (Fig. 2): (1) a metronome for controlling the rate of stepping; (2) a low rigid stand or platform, about 15 by 12 by 9 in. (38 by 30 by 22.8 cm.) high, whose height can be altered in ¼-in. (1.25-cm.) increments by placing the appropriate number of ¼-in. (1.25-cm.) boards on it; and (3) a low-resistance domestic type of gas-meter fixed to the platform at about elbow-height standing. This meter faces away from the patient using the step. It is modified by replacing its multiple small dials by a single large dial and pointer which is so geared that one revolution corresponds to 50 litres of gas passing through the meter, the dial being calibrated so that it can be read to the nearest half-litre. The pointer can be reset to zero manually. A mouthpiece and two-way valve are connected to the gas-meter by corrugated tubing from the valve outlet; the patient holds the valve in the hand while using the mouthpiece.

Procedure.—The patient is weighed and the step and metronome are each adjusted to the values selected from the nomogram. It is convenient to set the metronome at four times the stepping rate so that when exercise starts the left foot is raised on to the step in time with one click of the metronome, the right foot is then brought to it on the second click, the left foot returned to the ground on the third, and the right foot returned on the fourth, and so on. Using the metronome in this way makes it easier for the patient to keep time. While the test is being explained and demonstrated to him the patient rests in a chair. He puts on a nose-clip and gets used to breathing through the mouthpiece. The observer then records the cumulative readings of the gas-meter every half-minute for at least three minutes of rest. The metronome is started and the patient completes five minutes of exercise-stepping followed by about five minutes of recovery, during which he again sits at rest. During both the exercise and the recovery period the observer continues to record the half-minute meter readings until constancy in consecutive readings shows that recovery is complete.

Work-level Used.—For general purposes 350 kg.m./min. has been used for the five minutes of exercise. This level means that the exercise is not limited by muscle fatigue. It was chosen to provide enough exercise in fit subjects to provoke an accurately measurable ventilatory response, yet allowing the test to be completed by all but the most seriously disabled patients. Since the results can be expressed so that retesting at a lower level of work is unnecessary even if patients fail to complete the full five minutes of exercise (see below), this one work-level has been satisfactory. However, if only very seriously disabled patients were to be tested a lower level of work might be preferable.

Expression of the Results

In Fig. 3 the results of a typical exercise test in a normal subject are shown graphically in order to simplify description of the terms to be used. Differences between the successive cumulative readings of the gas-meter, which are the volumes of air exhaled in successive half-minute periods, have been plotted against time. The ventilation, which is constant at rest, increases during the first two or three minutes of exercise until a "steady state" is reached. When the exercise ceases the ventilation returns to the resting level. In patients who complete the exercise (the majority), with the venti-

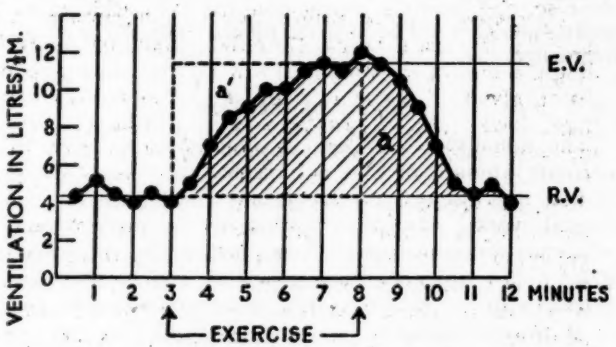

FIG. 3.—A typical result of the exercise test in a normal subject shown graphically to facilitate description of the terms used (see text). R.V.=Resting ventilation (ordinate × 2, litres/minute). E.V.=Exercise ventilation at a steady state (ordinate × 2, litres/minute). a=Area of replacement of ventilatory debt. (a' is an equivalent area.) Shaded area=Excess volume of air used as a result of the exercise (E.E.V.) Standardized excess ventilation (S.E.V.)= $\frac{\text{(E.E.V.)}}{\text{Time of Ex.}}$ i.e., average ventilatory cost (litres/min.) for each 350 kg.-m. of work done. Standardized ventilation (S.V.)=S.E.V.+R.V.

lation at a steady state, the "exercise ventilation" (E.V.) can be simply taken as a measure of the ventilation resulting from the exercise.

A few patients cannot, or will not, complete the full five minutes of exercise, and in these cases the E.V. is not an appropriate measure. However, in all patients the ventilatory cost of whatever work is done is the total increment of ventilatory volume during exercise and recovery above the initial resting level. This value, the "exercise excess volume" (E.E.V.), is represented by the area shaded in Fig. 3. Divided by the time of exercise it represents the average ventilatory cost of each 350 kilogram-metres (kg.-m.) of work which is completed. This average value is called the "standardized excess ventilation" (S.E.V.). The sum of the S.E.V. and the resting ventilation (which is comparable with the E.V.) is called the "standardized ventilation" (S.V.); it is an appropriate measure of ventilatory cost in all cases (see paragraph on the relation between the S.V. and E.V. below).

In practice the test results need not be graphed. The successive meter readings are recorded, together with their differences. The E.V. is then taken as the average difference in meter readings during the last three or four half-minutes of exercise over which the differences are approximately constant. This value is doubled, and so expressed in litres/minute. The S.V. is calculated as follows: the excess ventilatory volume of air used on account of the exercise (E.E.V.) is found by subtracting from the final meter reading the volume of air which would have been exhaled at rest during a corresponding period of time (the latter being got from the meter-reading at the end of the initial period of three minutes' rest by proportion); this volume is standardized by dividing by the time of exercise, and so expressed in litres/minute, and then added to the resting ventilation (R.V.). All gas volumes are expressed as saturated with water vapour at body temperature by multiplying by the appropriate factor given in Table I.*

Thus, in summary, the results obtained from the cumulative readings of the gas-meter as measures of the ventilatory cost of the work are: (1) the S.V., which is the sum of the S.E.V. and R.V. and is appropriate in all cases; and (2) E.V., which is simpler but appropriate only when the patient completes the full five minutes of exercise.

*It is assumed that the gas in the meter is at room temperature. This assumption is not quite true, but correcting for variations in room temperature in this way leads to negligible error.

TABLE I.—*Factors by Which Gas Measurements Recorded at Varying Room Temperatures are Multiplied for Correction to Body Temperature*

Temp. °C.	Factor	Temp. °C.	Factor	Temp. °C.	Factor
16 ..	1·119	21 ..	1·090	25 ..	1·069
17 ..	1·111	22 ..	1·085	26 ..	1·063
18 ..	1·107	23 ..	1·080	27 ..	1·057
19 ..	1·101	24 ..	1·074	28 ..	1·051
20 ..	1·097				

Relation Between the Standardized and Exercise Ventilation

The relation between the S.V. and the E.V. can be deduced from Fig. 3. Since the ventilatory debt, which accumulates at the beginning of exercise before a steady state is reached, is repaid quantitatively after the exercise ceases (Hill and Lupton, 1923), the area (a) can be represented by an equivalent area (a'), so that the excess volume of air used on account of the exercise (E.E.V.) is represented by the area outlined in dots. Hence in subjects who achieve a "steady state" the S.V. (which is represented by any one of the five rectangles between the minute abscissae during the exercise period and the upper dotted line of the E.E.V. rectangle) should be identical with the E.V. The agreement between the two is found to be very close in practice (see Fig. 5 and discussion of results).

But if a subject stops the exercise before a steady state is reached the S.V. will then be greater than any level of ventilation actually achieved. Thus, if the patient in Fig. 3 had elected to stop the exercise after only two minutes, when his ventilation was 9 litres in the half-minute, the

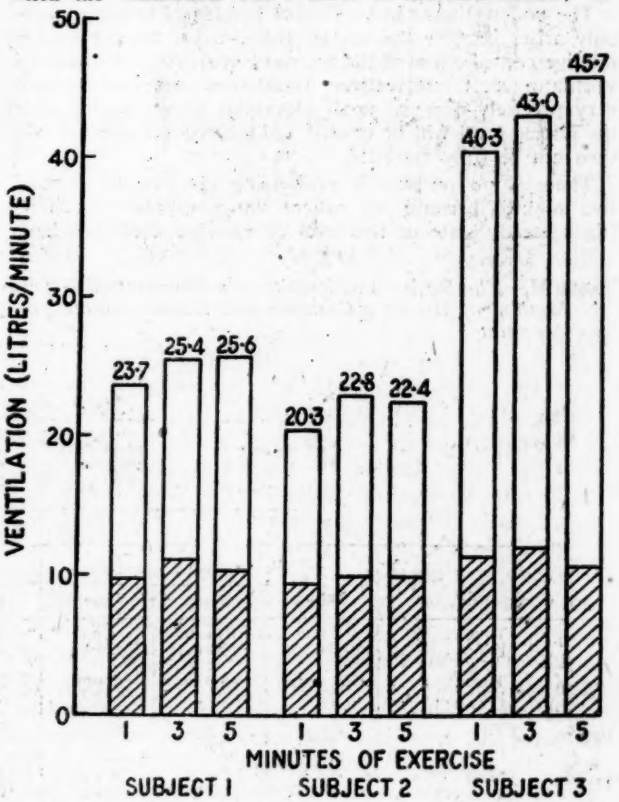

FIG. 4.—Results of standard exercise tests on each of two normal subjects and one with advanced emphysema (subject 3). All subjects did three tests with respectively one, three, and five minutes of exercise. Shaded rectangle=Resting ventilation (R.V.). Clear rectangle=Standardized excess ventilation (S.E.V.). Standardized ventilation (S.V.)—that is, S.E.V.+R.V.—is given in figures above each rectangle.

total ventilation in excess of the resting level would still represent the ventilation due to the exercise (though in this case only a total of 700 kg.-m. instead of the full 1,750 kg.-m.—350 kg.-m.×5 minutes), so that, when standardized, the ventilatory rate (or S.V.) would be the same as before.

When the level of exercise is an "overload," in a seriously disabled patient, the same argument applies: the ventilatory debt continues to increase the longer the exercise goes on; the patient is forced to stop, and pays back the debt by spreading an increase of ventilation over a number of minutes during recovery. The S.V. then represents a ventilatory rate greater than that which could be maintained or even achieved by the patient, for if this were not so a "steady state" rather than further debt could have been reached by continuance of the exercise.

Since the S.V. is theoretically independent of the time of exercise, why should we not be satisfied with less than five minutes of exercise? The reason is that small increments of ventilation over the resting level are difficult to detect. This point is demonstrated, and the above theoretical discussion justified, by an experiment in which two normal subjects and one subject with advanced emphysema, who could only just manage five minutes of exercise, performed three tests at the standard rate of 350 kg.-m./minute, but for one, three, and five minutes of exercise respectively. The results are shown in Fig. 4. It will be seen that the S.V. is reasonably independent of the time of exercise, though it tends to be smaller the shorter the exercise, so that when only one minute of exercise is performed it is an underestimate by about 10% of the value for five minutes' exercise. At three minutes there is an underestimate (5%) only in subject 3. Thus the standardized ventilation of subjects so disabled as to be unable to do more than three minutes of exercise at the low rate used in the test (a small minority in practice) is likely to be an underestimate of their ventilatory cost, which in these cases may be very large.

The underestimate in very short periods of exercise probably arises because the shorter the exercise the greater the relative contribution of the recovery ventilation to the total ventilatory cost, and recovery ventilation cannot be assessed very precisely because small elevations of ventilation over the resting level will be missed and the recovery period will then not be fully recorded.

There is no purpose is prolonging the exercise beyond five minutes, because any patient who is capable of achieving a steady state at the level of exercise used will have done so, and once this steady state has been achieved no greater precision will be obtained for the standardized excess ventilation.

Validity of the Test

The nomogram enables all subjects to be given a constant amount of external mechanical work, but is it true that subjects do a constant amount of physiological work? In other words, is the physiological efficiency the same over different portions of the nomogram? In order to determine this and to find the repeatability of the test, an experiment was designed as shown in Table II.

Three subjects, who were chosen to cover a fairly wide range in weights, performed the test daily during two periods of three days each. On each day the test was done three times (at 10 a.m., 2 p.m., and 4 p.m.) with different step-heights representing high, medium, and low values on the height scale of the nomogram, each height being used with the appropriate stepping rate to give the standard amount of work. The experiment was randomized as shown in Table II. The results of the experiment are given only in terms of the exercise ventilation, as all subjects completed the full five minutes of exercise and reached a steady state.

An analysis of these results is shown in Table III, in which the average values of the E.V. for comparable groups of results are given.

It will be seen from Table III that the method of standardizing the work is fully justified experimentally, since high, medium, and low heights of step, combined from the nomogram with appropriate slow, medium, and fast stepping rates respectively, lead to almost identical exercise ventilation rates. This experimental demonstration of the physiological validity of the nomogram confirms the conclusions of Passmore and Thomson (1950) that "stepping is a muscular movement with a very broad optimum of efficiency both as regards rate of stepping and height of step." They found a wide maximum of efficiency at rates between 14 and 18 steps a minute on a 10-in. (25-cm.) step.

TABLE II.—*The Design and Results of a Randomized Experiment Used to Determine the Validity and Repeatability of the Method of Giving a Constant and Known Amount of Exercise to Subjects of Different Weights When Performing the Step-test*

	Weight	Step Height		
		Low	Med.	High
	st. (kg.)	in. (cm.)	in. (cm.)	in. (cm.)
Subject 1 ..	14·04 (88·9)	9 (22·9)	10 (25·4)	11 (27·9)
,, 2 ..	10·04 (63·5)	10½ (26·7)	11½ (29·2)	12½ (31·7)
,, 3 ..	9·00 (57·15)	12 (30·4)	13 (32·9)	14 (35·4)

Date		Subject 1			Subject 2			Subject 3		
		High	Med.	Low	High	Med.	Low	High	Med.	Low
8/2/50	Time	2 p.m.	10 a.m.	4 p.m.	4 p.m.	2 p.m.	10 a.m.	10 a.m.	4 p.m.	2 p.m.
	E.V.	29·2	26·3	25·0	23·0	25·0	25·3	25·2	23·0	24·0
9/2/50	Time	10 a.m.	4 p.m.	2 p.m.	2 p.m.	10 a.m.	4 p.m.	4 p.m.	2 p.m.	10 a.m.
	E.V.	27·8	26·2	27·3	24·8	24·0	22·2	18·6	20·8	21·8
10/2/50	Time	4 p.m.	2 p.m.	10 a.m.	10 a.m.	4 p.m.	2 p.m.	2 p.m.	10 a.m.	4 p.m.
	E.V.	27·0	25·3	26·6	22·8	21·4	23·1	19·8	19·2	22·2
13/2/50	Time	4 p.m.	2 p.m.	10 a.m.	2 p.m.	10 a.m.	4 p.m.	10 a.m.	4 p.m.	2 p.m.
	E.V.	29·6	28·3	28·3	24·0	24·0	25·0	20·1	24·0	25·6
14/2/50	Time	2 p.m.	10 a.m.	4 p.m.	10 a.m.	4 p.m.	2 p.m.	4 p.m.	2 p.m.	10 a.m.
	E.V.	29·4	27·4	27·3	24·1	26·2	25·1	20·3	21·2	21·9
15/2/50	Time	10 a.m.	4 p.m.	2 p.m.	4 p.m.	2 p.m.	10 a.m.	2 p.m.	10 a.m.	4 p.m.
	E.V.	28·4	28·4	29·4	24·0	25·1	25·1	20·7	21·8	21·8

It is also seen from Table III that the test provides an objective measure of ventilatory cost which is highly repeatable, not being materially affected by the time of day or by variation between one day and another, though a full analysis of variance on the data showed the variance between days to be statistically significant.

TABLE III.—*An Analysis of the Results in Table II*

Step Height	High	Medium	Low	S.E. = 0·29
Av. E.V.	24·4	24·3	24·7	
Time of day	10 a.m.	2 p.m.	4 p.m.	S.E. = 0·29
Av. E.V.	24·5	24·8	24·2	
Day of test	8/2/50	9/2/50	10/2/50	S.E. = 0·41
Av. E.V.	25·1	23·7	23·0	
Day of test	13/2/50	14/2/50	15/2/50	
Av. E.V.	25·2	24·8	25·0	

Measurement of Breathlessness

We still have to relate the ventilatory cost of the standard exercise to the symptom of exertion dyspnoea. It is generally agreed that "breathlessness" is noticed with increasing severity the more nearly a subject's ventilation approaches the maximum of which he is capable. Thus to assess breathlessness on exertion the results of the exercise test must be related to the subject's maximum ventilation. The latter can be most conveniently measured on voluntary hyperventilation (Gray *et al.*, 1950, review the evidence for this), and it is then called the maximum breathing capacity (M.B.C.) or maximum voluntary ventilation (M.V.V.). Thus the relation between a patient's ventilation at a given state of exertion to the M.V.V. has been called a "dyspnoeic index": for if a patient's ventilation is only, say, 20% of his maximum, he is not very breathless, while if it is, say, 80%, then he is severely dyspnoeic. This, or a similar index, has been widely used by previous workers —for example, Kaltreider and McCann, 1937; Hannon, 1945; Warring, 1949; Baldwin *et al.*, 1949a, 1949b; Matheson and Gray, 1950; Pachner, 1950).

The Two Indices of Dyspnoea

By relating the results of the standard exercise test to the patient's M.V.V., two indices of dyspnoea are obtained:

The first dyspnoeic index ($D.I._1$) is that used by previous workers:

$$\frac{E.V. \times 100}{M.V.V.}$$

The second index ($D.I._2$) is the relation not of the exercise but of the standardized ventilation to the maximum:

$$\frac{S.V. \times 100}{M.V.V.}$$

The relation between these two indices is shown in Fig. 5, which is a scatter diagram of the results obtained from 228 subjects ranging from young normal men to men with severe pneumoconiosis, emphysema, and heart failure, so that all degrees of breathlessness on exertion are covered.

The value used for the patient's M.V.V. was the same in each index and was measured independently of the exercise test, all measurements being corrected to body temperature. The apparatus used has already been described (Gilson and Hugh-Jones, 1948–9).

It will be seen from Fig. 5 that in all patients who completed the full five minutes of exercise (185 out of the 228, shown as dots) the two indices agree very closely, the continuous line in the figure representing perfect agreement. This means, since the denominator

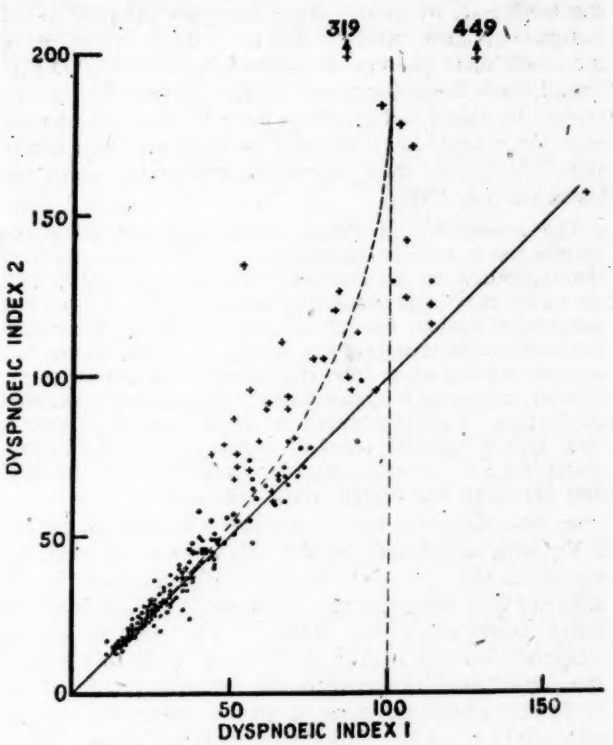

FIG. 5.—Scatter diagram showing the relation of the two alternative indices of dyspnoea obtained from the exercise test and measurements of the maximum voluntary ventilation (M.V.V.) on 228 subjects who covered a wide range of dyspnoea on exertion

$$(D.I._1 = \frac{E.V.}{M.V.V.} \times 100. \quad D.I._2 = \frac{S.V.}{M.V.V.} \times 100).$$

(Note: only 193 points are shown on this diagram, since the points would be superimposed in 35 out of the 228 subjects.)

of both indices is the same in any one patient, that the E.V. and S.V. are the same provided a steady state is reached; we have seen that this should be so theoretically.

Consider now the first dyspnoeic index (abscissae). First of all, by definition, this should not exceed 100%, since the M.V.V. is taken to represent the patient's maximum possible ventilation (Gray *et al.*, 1950). In fact, 10 of the 219 cases show an index greater than this. In these cases either full co-operation was not obtained in recording the M.V.V. or in a few very disabled men an exercise overload may create greater hyperventilation than the patient can bring himself to achieve voluntarily: these 10 patients were all very disabled and only two completed the exercise. Secondly, in subjects who do not reach a steady state an index obtained by using the maximum level of ventilation as a substitute for the true E.V. at a steady rate is false, for this ventilation results from less exercise than that of other subjects.

Now, if we consider the alternative $D.I._2$ (ordinates) it is evident that it may, and should, exceed 100% in a few cases. We have seen that very disabled subjects may spread a debt of ventilatory cost over a number of minutes which, when standardized by relating the total excess ventilation in exercise and recovery to the exercise time, gives a ventilatory *rate* (S.V.) greater than that of which they are capable.

It is probable that the subjects who failed to complete the five minutes of exercise and had a $D.I._2$ of below about 80% in Fig. 5 could have completed it and reached a steady state had they been prepared to tolerate

the feeling of dyspnoea, since an approximately equal number of such subjects did so. They would have increased their exercise ventilation, and their "D.I.$_1$" would have been increased to the correct figure. In those who failed and in whom the S.V. was greater than that which could have possibly been replaced at a steady state because of their maximum ventilatory limit, the index exceeds 100%.

The broken line in Fig. 5, about which all the points scatter, has been inserted, since it may aid the concept of the ventilation on exercise being unable to exceed a limit set by the maximum ventilatory capacity (100% D.I.$_1$). The continuous straight line of agreement between the indices means a steady state or "pay as you go"; the broken line represents a departure from this by stopping exercise as the limit of ventilation is approached and breathlessness becomes intolerable. A greater proportion of the ventilatory debt is then spread into the recovery period by those who fail, giving an S.V. increasingly large compared with the E.V. and hence an increasingly large D.I.$_2$.

In summary: by comparing the S.V., instead of the E.V., with a subject's M.V.V. we obtain an index of dyspnoea (D.I.$_2$) which is practically identical in all subjects who complete the 5 minutes' exercise with the index commonly used (D.I.$_1$). The new index of dyspnoea has the advantage of being applicable even if the subject fails to complete the exercise, provided two or three minutes are done to give a reasonably reliable estimate of the S.V.; thus the necessity for repeat testing at different exercise levels is avoided. When the subject cannot achieve a steady state, at the exercise level used, the D.I.$_2$ may exceed 100%.

Is the dyspnoeic index in practice related to the symptom of breathlessness? Kaltreider *et al.* (1937) found the usual index (D.I.$_1$) to be well related to subjective dyspnoea. Baldwin *et al.* (1949a) found "a clear-cut correlation between the severity of dyspnoea as recorded in each patient's history" and their "breathing reserve" (which is the complement of the D.I.$_1$—that is, $\frac{\text{M.V.V.} - \text{E.V.}}{\text{M.V.V.}} \times 100$) though subsequently Baldwin *et al.* (1949b) found the threshold of breathlessness on this index to be lower in cases of emphysema than in other patients. However, in their index the ventilation during the first minute of recovery after only one minute of exercise is used as an expression of exercise ventilation.

In our 228 subjects the indices showed a general relation to symptomatic "breathlessness." Fig. 6 is a scatter diagram relating the D.I.$_2$ to the clinical grading of the patients into four approximate grades of breathlessness by Dr. C. M. Fletcher on the basis of the following standard questions:

Grade 1: Is patient's breath as good as that of other men of his own age and build at work, on walking, and on climbing hills or stairs?

Grade 2: Is patient able to walk with normal men of own age and build on the level but unable to keep up on hills or stairs?

Grade 3: Is patient unable to keep up with normal men on the level, but able to walk about a mile or more at his own speed?

Grade 4: Is patient unable to walk more than about 50 yards on the level without a rest?

Grade 5: Is patient breathless on talking or undressing, or unable to leave his house because of breathlessness? (Not used for test.)

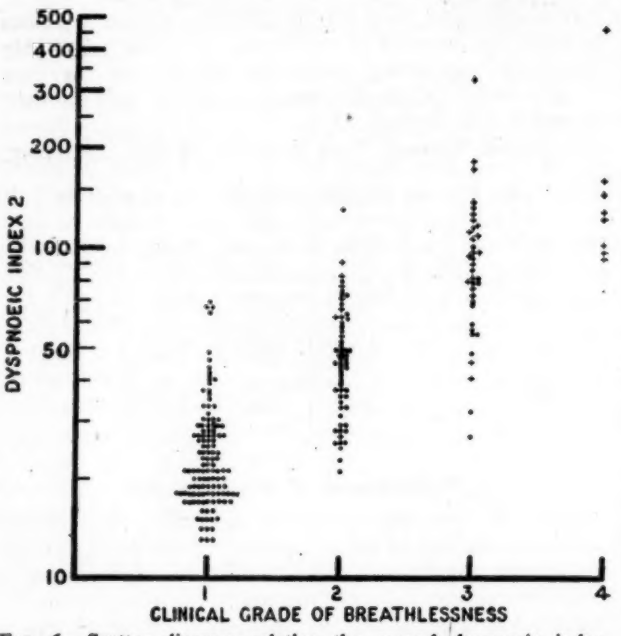

FIG. 6.—Scatter diagram relating the second dyspnoeic index (D.I.$_2$) of 228 subjects to a grade of "breathlessness" as determined independently from clinical history.

There is a general agreement between the measured dyspnoeic index and patient's reply to the questions about his breathlessness.

The dyspnoeic index is plotted on a logarithmic scale for convenience. On a "straight" plot the relation between index and grade is non-linear, patients in the lowest clinical grades often having particularly large indices of dyspnoea. This effect may be due to the scale of grading, since scales of judgment are frequently non-linear. Moreover, on a straight plot there is a skewed distribution within each grade, especially in the first, which may have resulted from the dyspnoeic index having a limiting value of about 12% at the lower end, which represents the minimum ventilation at this level of exercise.

Normal Values.—Since the exercise results (the E.V. and the S.V.) are compared with the subject's M.V.V. to give an objective measure of breathlessness their "normality" *per se* does not arise. However, since one may wish to know whether a patient's exercise ventilation itself is excessive or not—for example, in the assessment or treatment of heart failure as is discussed below

TABLE IV.—*Average Value of the E.V. and S.V. Resulting from the Exercise Test, Together with the Corresponding Indices of Dyspnoea, in Four Different Age Groups of Normal Subjects and a Group of Athletes (Numbers in Parentheses Represent the Range of Values Found)*

Age	No. of Subjects	M.V.V.* (l./min.)	E.V. (l/m.)	D.I.$_1$ $\left(\frac{\text{E.V.}}{\text{M.V.V.}} \times 100\right)$	S.V. (l./m.)	D.I.$_2$ $\left(\frac{\text{S.V.}}{\text{M.V.V.}} \times 100\right)$
Athletes (O.U.A.C.) 23 years ..	17	187 (156–228)	30 (24–35)	16 (12–20)	27 (19–34)	15 (11–18)
Normal subjects 25 years ..	10	151 (125–178)	25 (19–33)	17 (11–26)	27 (22–33)	18 (13–27)
35 years ..	10	145 (75–176)	25 (19–36)	18 (13–25)	26 (20–37)	19 (14–29)
45 years ..	10	131 (102–149)	24 (20–30)	18 (13–27)	25 (22–30)	20 (14–23)
55 years ..	10	118 (83–157)	26 (22–31)	22 (16–28)	28 (21–38)	24 (18–30)

* Subsequent re-calibration of the M.U.V. apparatus shows these results may be slightly high. The error does not affect the conclusions.

—the values in 40 "normal" subjects, 10 in each of four age groups, is given as Table IV. The normal subjects were men most of whom were temporarily attending the Ministry of Labour's Employment Exchange in changing from one job to another. Only men with abnormal chest radiographs, hypertension, or clinical evidence of heart or renal disease were excluded. The results of testing 17 medium-distance runners of the Oxford University Athletic Team, whom we examined through the kindness of Dr. R. W. Parnell when he was investigating their physique (Parnell, 1951), are also included as the upper limit of "normality." It will be seen that the E.V. and S.V. are a very stable value not related to age, and decline in the dyspnoeic index, associated with the increasing breathlessness of ageing, is due to decrease in the ventilatory reserve as measured by the M.V.V.

Discussion and Conclusions

When this standard exercise test is to be used for measuring breathlessness it should ideally always be combined with some independent measurement of the patient's maximum ventilation such as the M.V.V., because breathlessness may arise either from a reduction in the maximum or from an increase in the exercise requirements, and only the latter can be measured by the test. In coal-workers' pneumoconiosis, for example, abnormal breathlessness on exertion, the cardinal symptom of the disease, is almost entirely due to reduction in the ventilatory capacity; excessive exercise ventilation does occur, however, mostly in men who have some evidence of right-sided heart failure (Gilson and Hugh-Jones, 1952), so that in this disease the exercise test is necessary to avoid error which would arise if the maximum voluntary ventilation alone were used for the objective assessment of breathlessness. In general cases of heart failure, on the other hand, abnormal E.V. is an important cause of breathlessness, and may be one of the earliest signs even when oxygen consumption is still normal (Harrison and Pilcher, 1930). In this case the measurement of the S.V. by the exercise test may itself provide a convenient objective method of assessment, though it should be supported by tests of maximum ventilatory capacity if occasional error is to be avoided.

One obvious effect, which might be thought to lead to error in the test, is hyperventilation through nervousness, mouthpiece resistance, etc. It certainly may cause an increased resting ventilation (R.V.) and then an apparently small exercise excess volume of air (E.E.V.). This means that the latter, which might otherwise be used as a measure of the test efficiency of the subject, may be erroneous. However, this reciprocal relation between the increased resting ventilation and the diminished volume of air caused by the exercise is such that their sum, the S.V., remains correct. Many cases of "nervous" hyperventilation occurred in the normal subjects among the 228 men examined and reported here, yet it was seen from Fig. 4 that their S.V. and E.V. agreed very closely.

In conclusion, the exercise test described in this paper has advantages in providing a known amount of work for the subject, comparable with a bicycle ergometer, but using only simple apparatus; a "submaximal" test which is not distressing for the patient or as time-consuming for the observer as testing maximal response; a valid quantitative result in the S.V., whether the patient completes the test or not provided two or three minutes of exercise is done. The S.V. is little disturbed by subjective influences, and its use means that repeated exercise tests are not required, as they are when the amount of work is varied to give a constant response.

Summary

A simple step-test is described which enables a patient to be given a known and standard amount of exercise, comparable to exercise on a bicycle ergometer, without the use of complex apparatus. The standard exercise is achieved by adjusting both the height and the rate of stepping to compensate for variations in weight between one patient and another, the appropriate values being got from a nomogram without calculation.

The exercise period is five minutes. A suitable work load is usually 350 kg.-m./minute.

The patient's ventilatory response is recorded with a domestic gas-meter. This is expressed as a "standardized ventilation" (S.V.), which is got from the ventilation in excess of the resting level during both exercise and recovery and gives a valid measure even if the patient cannot or will not complete the five minutes' exercise. In all subjects who complete the test the S.V. is numerically equal to the exercise ventilation (E.V.) at a steady state.

For measuring the symptom of breathlessness the ventilation caused by the exercise should be related to the patient's maximum voluntary ventilation (M.V.V.) measured independently. A dyspnoeic index $\left(\frac{\text{S.V.}\times 100}{\text{M.V.V.}}\right)$ is suggested as an alternative to the index previously used by other workers—namely, $\frac{\text{E.V.}\times 100}{\text{M.V.V.}}$. The former index avoids the necessity for repeat testing at a lower exercise level in those who fail to complete the exercise, when the usual index becomes invalid.

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LATE RESULTS OF PERURETHRAL PROSTATIC RESECTION

BY

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Advances in the open surgery of prostatic obstruction have distracted attention from the merits of the perurethral approach. Harris (1929) and Wilson Hey (1946) have shown the advantages of closing the bladder, and Millin (1945) has demonstrated the advantages of not opening the bladder at all. Surely it is better still to leave the abdominal wall intact.

The immediate results of perurethral prostatic resection are recognized to be good. This operation has a very low mortality, and its value in this respect is greater than can be shown by figures, for many general surgeons enucleate the straightforward case themselves but refer the "bad risk" to the urologist for perurethral treatment. The use of thrombin has eliminated the frequent wash-outs of the bladder which were considered necessary and has reduced enormously the incidence of clot retention. Suction evacuation has shortened the duration of the operation and facilitated the treatment of larger glands. Isotonic irrigating fluids have eliminated post-operative anuria—never a common complication, but a grave one. Many patients experience merely the minimal discomfort associated with a modern anaesthetic and a few days of catheter drainage. The present investigation is an attempt to assess the late results, on which the reputation of this operation clearly depends.

Indications

The patients were treated by the "punch" type of operation, using the Gershom Thompson resectoscope. This is the operation which has achieved superlative results at the Mayo Clinic. The indications varied a little at different times, but a high proportion of the patients were treated perurethrally throughout. In the last 400 cases referred to the urological units at the Victoria Infirmary and Hairmyres Hospital the mortality was 3.25% (13 cases). Table I shows all cases of prostatic enlargement referred to these units during the same period and gives an impression of our present practice. "Expectant treatment" includes those cases referred on account of prostatic enlargement without signs of obstruction and with only mild symptoms. This group has been discussed more fully elsewhere (Chapman, 1949). "Endocrine treatment only" includes cases of carcinoma of the prostate in which obstructive symptoms were not marked. "Catheter drainage only" includes cases in which bladder function was resumed after a short period of catheter drainage, and in which the patient refused operation or was advised against it. Several of these were cases of acute retention in the post-operative phase of some other condition.

TABLE I.—*Treatment of All Cases of Prostatic Enlargement*

Expectant treatment	138 cases
Endocrine treatment only	27 "
Catheter drainage only	9 "
Perurethral resection	400 "
One-stage suprapubic prostatectomy	18 "
Two-stage " "	11 "
Retropubic prostatectomy	5 "
Permanent suprapubic cystostomy	26 "
Catheter drainage (admitted in extremis)	23 "

Suprapubic prostatectomy was performed when the gland was exceptionally large, or when complicated by large diverticula, or when the urethra would not accommodate the instrument with ease. When stones accompanied prostatic obstruction, litholapaxy and prostatic resection were performed if both the stone and the prostate were of moderate size. Four of the five retropubic prostatectomies were performed by a deputy doing holiday duty. Permanent suprapubic cystostomy was advised for the "very bad risk" patient. The final item of the Table includes patients whose prostatic obstruction proved to be only an incident in the final stage of some other disease. Of all patients whose prostatic disease was severe enough to require operation and whose general condition justified the removal of the obstruction, 92% were treated by perurethral prostatic resection.

Description of Present Investigation

In this investigation we are concerned with late results, and patients treated since 1949 are not included. Efforts have been made to maintain contact with all patients. Postal questionaries were sent out on five occasions—December, 1941, April, 1945, June, 1946, August, 1948, and August, 1950. Patients who had changed their address or who failed to respond were usually traced by the almoner's department of the Victoria Infirmary. If the reply to a questionary suggested unsatisfactory progress the patient was asked to attend for examination. In 1948 an attempt was made to see all surviving patients. Of the 497 patients traced, 28 died within a year of operation and are not considered except in the discussion of cause of death. In six cases in which the operation was performed in the hope of removing a suprapubic tube an unsatisfactory result was obtained and the tube was retained. In two cases frequent micturition persisted after the operation, and the patient sought advice elsewhere. In both cases an enucleation operation was performed and the frequency persisted. The convenient explanation was given that damage had been caused by the perurethral resection. Both were cases in which frequent micturition was the chief symptom and the evidence of obstruction was not great. It is sometimes justifiable to operate for frequent micturition alone, but it is common experience that disappointing results occur in this group.

The remaining 461 cases are tabulated in Table II. In the cases of nodular hyperplasia an attempt was made to remove all glandular tissue. No doubt this has been

TABLE II.—*Duration of Follow-up*

Duration in Years	Cases of Nodular Hyperplasia	Cases of Median Bar	Cases of Carcinoma	Total No. of Cases
13+	1	—	—	1
12–13	9	—	—	9
11–12	10	—	—	10
10–11	13	—	—	13
9–10	12	5	—	17
8–9	22	2	2	26
7–8	22	2	—	24
6–7	26	2	—	28
5–6	34	3	3	40
4–5	39	3	4	46
3–4	39	3	2	44
2–3	68	5	13	86
1–2	100	6	11	117

more successful in the later than in the earlier cases. In the median bar cases only a small quantity of tissue was removed. In the carcinoma cases variable quantities were removed, sufficient to produce a wide channel. Since 1942 these patients have also received stilboestrol treatment. Table II shows the duration of follow-up—that is, the period between operation and the time of writing in the case of survivors, or the period between operation and the date of the patient's death.

Deaths During Follow-up

Table III shows the cause of death in those patients who died within a year of operation and who have not been considered in the general discussion. It is probable

TABLE III.—*Cause of Death Within One Year of Operation*

	Nodular Hyperplasia	Carcinoma
Urinary infection	2	—
Uraemia	2	—
Secondary prostatic carcinoma	1	2
Cardiovascular disease	9	—
Carcinoma (extraurinary)	3	1
Cerebral thrombosis or haemorrhage	3	—
Pneumonia	1	—
Obstructive jaundice	1	—
Infective hepatitis	1	—
Unknown	2	—

that the original condition or the operation for its treatment was responsible for death in the four cases in which death was due to urinary infection and to uraemia. In one case in which the prostate was apparently benign at the time of operation and in two cases in which malignancy was known to be present the patient died of secondary malignant disease. In the remaining cases there appeared to be no association with prostatic obstruction or its treatment.

Table IV shows the cause of death in those patients who have survived more than a year. In nine cases death was due to urinary infection or to uraemia, and these again must be associated with prostatic disease. One patient who had an apparently benign prostate and five who had definitely malignant prostates died of secondary carcinoma. In the remaining cases there was no obvious connexion.

TABLE IV.—*Cause of Death in Those Surviving More Than a Year*

	Nodular Hyperplasia	Carcinoma	Median Bar
Urinary infection	7	1	—
Uraemia	1	—	—
Secondary prostatic carcinoma	1	5	—
Cardiovascular disease	33	3	2
Carcinoma (extraurinary)	13	—	—
Cerebral thrombosis or haemorrhage	11	—	—
Pneumonia	3	—	—
Nephritis	2	—	1
Anaemia	2	—	—
Carcinoma of bladder	1	—	—
Ascites	1	—	—
Diabetes	—	—	1
Disseminated sclerosis	—	—	1
Septicaemia	—	—	1
Duodenal ulcer (haematemesis)	1	—	1
Accident at work	1	—	—
Strangulated femoral hernia	1	—	—
Ulcer of back	1	—	—
Unknown	8	2	3

Results in General

In most cases the patient was very well pleased with the function of the bladder. The results as judged by day and night frequency, force of the flow, control of the flow, and the effect on general health were excellent throughout the period of observation. If doubt arose bacteriological examination of the urine, intravenous pyelography, and endoscopic examinations were performed. Complications have occurred, and these are considered individually.

Recurrent Prostatic Obstruction

Many believe that the effects of perurethral prostatic resection are temporary or even brief. For example, Grant and Lich (1948) write about the "enormous percentage" of recurrent cases, and we have been asked quite seriously how many times it is necessary to repeat this operation in the course of a year in order to keep a patient free from obstruction. This impression is often due to confusion between benign prostatic enlargement and an active malignant process where a few cells left behind will grow in an uncontrolled manner. It has been shown by Moore (1936, 1943) that the process of involution in the prostate goes on with the greatest rapidity before the age of 60, and that the aetiological agent which produces benign hyperplasia is most active before that age. One of us has demonstrated this fact in a follow-up, extending over ten years, of patients who had received no treatment at all (Chapman, 1949).

In the group of patients discussed here 18 have had a second operation for recurrent prostatic obstruction, and to these must be added five patients who had been operated on elsewhere, probably for obstruction, and two patients treated in other units in whom obstruction is known to have occurred, although no operation was advised. Two patients who had previously had resection for median bar returned after intervals of seven and ten years, showing signs of obstruction which proved to be due to lateral lobe enlargement; there was no evidence of recurrence of the bar formation, and the lateral lobes had enlarged during the interval. These two cases need not be considered in a discussion of recurrence of benign prostatic enlargement.

The incidence of recurrence was much higher in patients followed up for more than ten years. This is not due merely to the longer follow-up. In the earlier stages of his experience an operator removes less tissue. In the units discussed here 14 g. was an average resection in 1938; 50 g. resections are now fairly common. Of 116 cases of benign hyperplasia followed up for a period of five to ten years, seven have recurred, a rate of 6%. This is much lower than is usually suggested by the detractors of this operation. Of 246 cases of benign hyperplasia followed up for one to five years, five (2%) recurred. This is a clear demonstration of the great value of the operation in patients whose expectation of life is short. Local recurrence of obstruction in malignant cases has not been common. Possibly stilboestrol treatment is responsible to some extent for this. It must be noted, however, that only two malignant cases survived for more than six years.

Most urological surgeons treat many of their papilloma cases by multiple perurethral diathermy treatments, yet suprapubic, perineal, and retropubic prostatectomists join in their cries of horror at the thought of a second resection of prostatic tissue, however small. This would be less surprising if the open operations were free from the risk of recurrence themselves. Millin (1942) found in his records 53 cases of post-prostatectomy obstruction after suprapubic operations by various surgeons. Emmett (1944) found records of 102 patients who had suffered from recurrent obstruction after suprapubic and perineal operations. The retropubic operation, so recently devised, has already had recurrences.

By far the most important point about recurrence after perurethral prostatic resection has yet to be mentioned. In most cases the correction of the recurrence is a trivial matter both for the surgeon and for the patient. The amount of tissue to be removed is quite small and the operation quite short. With one exception these operations for recurrent obstruction have been free from trouble, and most of the patients have not regarded the experience as a surgical operation.

Second Operation for Symptoms other than Obstruction.—Six patients have had a second operation for reasons other than obstruction. One patient had attacks of haematuria at intervals, and it was thought that the removal of a few remnants of prostate might reduce this tendency. He continues to have occasional haematuria, though his general health is good. Four had persistent frequent micturition, and a second resection was performed in the hope of relieving this. Some benefit resulted in these cases, though there was no evidence of recurrent obstruction. One patient who had heavily infected urine before his operation did not improve much after his resection, so a second small resection was tried, also without much effect.

Post-operative Stricture

Millin (1947) comments on the "high incidence" of post-operative stricture after perurethral prostatic resection, and Grant and Lich (1948) describe it as a "frequent sequela." In the present series of 461 cases nine post-operative strictures have occurred. Two of these required to have the stricture excised and one had an external urethrotomy. All attend at intervals for bougie dilatation; in three cases the interval has been extended to one year. The most recent answers to questionaries in these nine cases show that six have no difficulty in micturition, one has some difficulty in the morning, and two notice a weakening of the flow before they attend for bougie treatment. One of them passes urine at intervals of two hours; the others have intervals of three or more hours. This complication is not a major catastrophe, but it is a very unpleasant experience, and all steps should be taken to avoid it.

Urethral bougies passed without force do not influence the calibre of the normal urethra, but they seem to facilitate the passage of the resectoscope. This may be the result of thorough spreading of the lubricant. They also show when the instrument ought not to be passed. For many years American surgeons have used resectoscopes through a perineal stab when the lumen of the urethra was not adequate. An unfounded fear of fistula formation deterred us from the use of this method for many years. Recently, on the strong recommendation of T. J. D. Lane, we have used it with success.

Incontinence of Urine

Urinary incontinence has occurred after all types of prostatic operation and is said to be commoner after perurethral procedures. The present investigation appears, at first glance, to support this view, as seven patients require to wear incontinence bags. This impression is modified by further consideration. Three of these patients had carcinoma of the prostate and were incontinent before their operation. The disease rather than the operation appears to be responsible in these cases. The same may be said of another patient who had an infected prostate and was referred by a general surgeon who would have enucleated an uninfected gland. In another there was gross fibrosis of the prostate and of the region around the bladder neck as a result of old infection. A minute resection from a prostatic bar increased the incontinence of another patient: the cause is probably neurogenic, though no definite evidence has been found. The remaining patient, a case of simple nodular hyperplasia, is probably the only one in the series in whom an enucleation was a reasonable alternative.

One patient who had persistent incontinence after resection was treated with complete success by the operation described by Millin (1939). Two other patients have had this treatment without success.

In addition to these patients a few have a slight dribbling after the act and find it convenient to wear a pad. One man gives the unusual story that his control is excellent except when he goes to sleep in a chair—a practice which could be avoided without serious results.

It is true, however, that many patients are incontinent for a few hours or days after the removal of the catheter, and in some cases this symptom has persisted for a few weeks. The detrusor has hypertrophied to overcome the obstruction, and the sudden removal of the obstruction has left the sphincter at a disadvantage. The movements of the instrument produce some stretching of the sphincter, which is sufficient in some cases to retard the recovery of its tone.

Conclusions

The complications of perurethral prostatic resection have been exaggerated, and this operation is worthy of a greater place in the treatment of prostatic obstruction in this country. Many British surgeons use perurethral resection only in fibrous prostates, malignant prostates, and "bad risk" cases, and believe that the functional result after perurethral resection is, in general, inferior to that of an enucleation operation. Perurethral resection is selected for these groups only because enucleation is impossible. The best results by the perurethral methods are obtained in the small or moderate glandular types. The distinction between gland, bladder neck, and capsule is clear, and removal of the glandular tissue is an exact procedure. It is true that the removal of the very large gland is an extremely difficult operation, but a gland of 20–40 g. can be removed in a reasonable time, with negligible upset to the patient, by a surgeon who has been trained in this operation. We believe that the indications should include such cases, and that these constitute the majority of patients suffering from prostatic obstruction.

The open operations for prostatic obstruction have become much safer in recent years. This is one reason for the decrease in interest in perurethral operations. It is not, however, an adequate reason. It is instructive to compare the treatment of vesical calculus. The crushing of a bladder stone is a very old operation, and when it became reasonably safe to open the abdomen interest in litholapaxy decreased. The urological specialist continued to practise it, however, and there is no doubt that it is still the operation of choice for the usual bladder stone of moderate size. The only reason for another course is the absence of any surgeon experienced in the operation.

In prostatic surgery in this country it is usual to reserve perurethral resection for the case in which enucleation would be difficult or impossible. We believe that the opposite policy might be employed with

advantage—that is, to use enucleation operations only when there is a serious contraindication to the perurethral route.

Summary

Perurethral prostatic resection has been used in the treatment of over 90% of patients fit for the removal of prostatic obstruction.

We followed up 461 cases for periods of one to thirteen years, and in the great majority an excellent functional result has been maintained throughout.

Recurrent prostatic obstruction occurred in 6% of cases of benign hypertrophy followed for five to ten years and in 2% followed for one to five years.

Post-operative stricture occurred in 2% of cases and was not difficult to treat.

The operation failed to relieve incontinence in five cases and produced incontinence in two—one a nodular hyperplasia and the other a fibrosis of the prostate and periprostatic tissues of inflammatory origin.

The results suggest that the complications of perurethral prostatic resection have been exaggerated, and that this operation is worthy of a much larger place in British surgery.

Our debt to the surgeons of the Mayo Clinic is obvious. In addition we wish to thank Dr. A. B. M. Currie, Dr. W. Kraszewski, and the staff at the Victoria Infirmary, Glasgow, and Hairmyres Hospital, Lanarkshire.

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INCONTINENTIA PIGMENTI

REPORT OF CASE, WITH SUMMARY OF 29 CASES FROM THE LITERATURE

BY

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Twenty-six years ago Bloch (1926) demonstrated to the Swiss Dermatological Society at Basle an 18-months-old girl with irregularly distributed bizarre-shaped pigmentation of slate colour involving the trunk and lower extremities. After histological study of the skin he gave the condition the name of incontinentia pigmenti. In 1925 Bardach had reported "systematized naevus-formation" in a pair of 17-months-old twins, undoubtedly with the same condition. Since 1926 at least 29 other cases have been reported, the details of which are summarized below. Although reports have come from Germany, Sweden, the United States (both white and black subjects), Canada, Holland, Denmark, and Japan, no case has yet been recorded in England. It is true that Kalz and Mackenzie (1947) published a case in the *British Journal of Dermatology and Syphilis*, but the child was Polish and in Montreal.

The case reported here is that of a baby who was born and lives in Hertfordshire.

Case Report

A female infant, born on February 24, 1950, was the survivor of first-born twins, eight weeks premature, the other twin being stillborn. The mother and father are unrelated, are both healthy, and there is no family history of skin disorder. The mother's father and her younger brother were each blind in one eye from babyhood. Neither survives, and the nature of the blindness is unknown.

The patient weighed 3 lb. (1.4 kg.) at birth, but was rather feeble. I saw her in her first week for this reason, and she remained in hospital for five weeks. During this time her skin was normal. Except for the skin condition described below she has been a normal girl and free from symptoms. When aged 2 months the left lower limb became swollen and red, and when two or three days later the swelling subsided a "scorch-mark" was seen by the mother. At 7 months there was another attack, the child becoming ill-at-ease and feverish, and seeming to be in pain. The left lower limb became swollen, red, and shiny; after three hours blisters appeared in the pigmented areas and a measles-like rash on the clear skin. A few days later the swelling subsided and further pigmented areas were found. When I saw her at 13 months (March 28, 1951) there had been three attacks and the lower limbs only were affected. Three

FIG. 1.—Showing the pigmentation on the chest and the narrow stripes round the trunk.

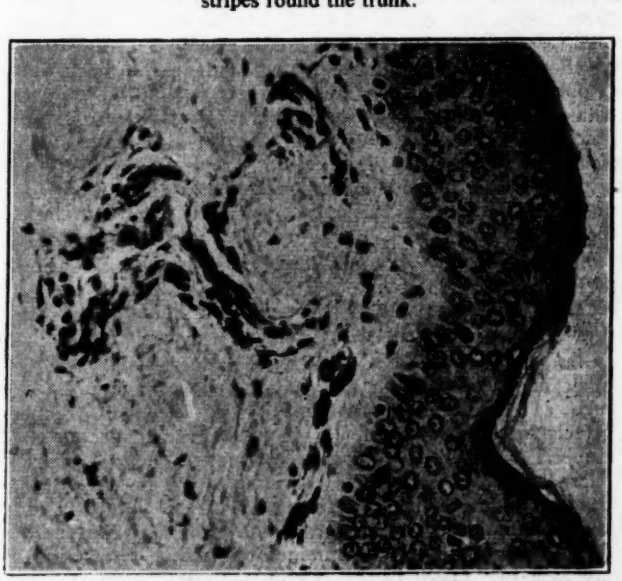

FIG. 2.—Section of skin showing a large number of melanophores containing closely packed melanin granules. (×240.)

months later, after further attacks, there was reticulated dark-brown pigmentation on the chest and abdomen.

Being quite unfamiliar with the appearance, I referred her to my dermatological colleague at St. Bartholomew's Hospital, and Dr. Brian Russell suggested the correct diagnosis.

The child is making normal progress, though her weight is only 18 lb. (8.2 kg.) at 20 months. There are no abnormal pigments in the urine. Hair, teeth, nails, and eyes are normal. There is as yet no sign of fading.

Fig. 1 shows the curious pigmentation, with the particular concentration on the chest, characteristic of the condition. There are many parallel transverse narrow stripes round the trunk. Dr. Cureton has reported as follows on a biopsy specimen of skin taken from the left chest wall by Mr. R. S. Murley: "Sections of the skin show no gross structural changes. The amount of melanin pigment in the basal layer of the epithelium is variable—one section shows a moderate amount, another shows virtually none. All sections show a large number of melanophores containing closely packed melanin granules and situated almost entirely in the superficial corium. The appearances are those described in incontinentia pigmenti" (Fig. 2).

Summary of Cases

Twenty-nine case reports in the literature have been studied and are summarized, together with the thirtieth case, described above.

Sex.—Twenty-six are females, three are males, and the sex in one is not stated.

Condition of the Skin.—At birth:—18 were normal, 5 had erythema with or without blisters, 2 had actual pigmentation, and 2 others had a pigmented naevus. The condition in 3 is not stated. *In the neonatal period:*—Skin lesions were reported in 11 cases (erythema in 8, skin sepsis in 3). *Pigmentation* was present at birth in 2 cases, and developed from a skin lesion or *de novo* within the first month in 9 cases, before the age of 6 months in 6 more cases, and by the age of 3 years in a further 11. The 2 remaining cases were the father of two other cases and a girl first seen at 6½ years. *Colour* is variously described as steely grey or blue, slate-grey, dark brown, light brown, or café-au-lait. Several colours may be seen in one case. *Distribution:*—The upper part of the lower limbs and the trunk, particularly in the breast region, are most often and most heavily affected, and the lower part of the lower limbs and the upper limbs less often. Lesions of the scalp have twice been recorded. In two cases (Bardach, 1925; Siemens, 1929) a yellowish band of pigment was found on the face; and in one (Fleck, 1950) there were pigment patches on the soft palate. Sometimes the distribution is symmetrical; sometimes one side of the body is more marked than the other. *Fading* is reported in 12 cases, all but one being over the age of 3 years. No comment is made in 2. In 16 there was no fading, but 9 of these were under the age of 3 years at the date of the report.

Family History.—A family history of pigmentation occurs in Bardach's (1925) twins, who were both affected, and in Nägeli's (1927a, 1927b) father and two daughters. The present case is one of twins, the other being stillborn.

Associated Congenital Defects.—Nineteen cases have no other abnormality. Six have some congenital eye defect, such as pseudo-glioma or opacity of the lens. Other defects noted are brittle or spoon-shaped nails, patchy alopecia, dental hypoplasia, congenital heart disease, microcephaly, and spastic paraplegia. The record of congenital defects in other members of the family is certainly incomplete. Sulzberger *et al.* (1938) give a family tree showing congenital blindness in many females. In my case two males in the family had some form of congenital blindness.

Histology.—The most striking feature of the histological picture of the established condition is the collection of melanin pigment in the chromatophores of the corium, often arranged round the blood vessels. There is also a disarray of the basal cells of the epidermis. In scattered areas the regular line of these cells is broken, and individual cells are seen to be small or distended and vacuolated, with deficiency or absence of the normal pigment granules. The nuclei may be pyknotic. In the earlier stage of the disease there is some oedema of the skin, with vesiculation and perivascular cell infiltration (Haxthausen, 1944). In one post-mortem report (Seidlmayer, 1942) the adrenal medulla was aplastic.

Discussion

The explanation given by Bloch (1926) is that the melanin pigment in the skin, instead of leaving the basal layer and passing out into the stratum corneum to be flaked off in wear and tear, behaves "incontinently" and descends into the corium, where it is gathered up by the chromatophores and produces "autochthonous tattooing." There is no excess of melanin production. Bardach (1925), whose cases are the earliest known at present, regarded the condition as a form of systematized naevus. Nägeli (1927a, 1927b) used the name "familial chromatophore-naevus." Siemens (1929), who gives a very clear and careful account of the histology, regarded the basal layer lesion as the primary defect and suggested the title "melanosis corii degenerativa" as a description of what was seen in the skin section in preference to Bloch's name, which described a theory of production that might prove mistaken. He believed that this is an idiopathic example of degenerative melanosis which can occur under other circumstances, such as in parapsoriasis and poikiloderma.

Incontinentia pigmenti is a disorder of the skin arising at or soon after birth or in the early months of life, and usually in girls. It would be interesting to know how many of these subjects have been small or premature. Heilesen (1948) has stressed that there are three stages of the disorder, but that in some cases only the second stage may be present. First there is erythema with some papule or vesicle formation. Then when this subsides the affected area is noticed to be pigmented. Periodic attacks leave pigmentation more and more widely spread. In some cases the pigmentation appears in skin previously normal. The third stage—fading—may be incomplete or absent. At its height the pigmentation is found on the trunk and lower limbs in all cases. Upper limbs and scalp may be affected, as may the oral mucosa. Two cases had curious yellowish bands of pigment on the face. The colour is sometimes grey or steely blue or some shade of brown, several colours occurring in one case. The pattern is symmetrical, but often one side is more heavily involved than the other. All writers describe bizarre shapes, tree-like branching, and, round the subject's trunk, parallel lines giving a superficial and erroneous suggestion that nerves are followed.

A congenital defect of the eye or an ectodermal defect may be present in the case or in some member or members of the family. Other members of the family may have incontinentia pigmenti.

The familial character and the association with other recognized congenital ectodermal defects supports the view that this is a congenital abnormality of the skin.

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CONGENITAL DUODENAL OBSTRUCTION AND MONGOLISM

BY

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We have recently been impressed by the frequency with which intrinsic obstruction of the duodenum in the newborn has been associated with mongolism. During the past 25 years 32 infants with congenital atresia or severe stenosis of the duodenum have been admitted to Great Ormond Street, and of this number no fewer than 10 were recognized as mongols.

Case Reports

Case 1.—A first-born male child, three weeks premature. Mother aged 25. Admitted aged 6 weeks because of vomiting and constipation from birth. *Clinical diagnosis:* Mongolism and pyloric stenosis. *Operation:* Gastro-enterostomy for apparent "duodenal ileus." Death occurred a few hours after operation. *Necropsy:* Mongolism; stenosis of third part of duodenum, peritonitis, and organized pleurisy.

Case 2.—A male child, tenth in family, born at seven months' gestation. Admitted aged 2½ days with imperforate anus, severe vomiting, and deep jaundice with purpura. *Clinical diagnosis:* Mongolism with anal atresia. *X*-ray film suggested possible duodenal atresia. *Operation:* Relief of anal atresia. Death occurred the following day. *Necropsy:* Mongolism; atresia at junction of second and third parts of duodenum; large subarachnoid haemorrhage.

Case 3.—A full-term male child, second in family. Admitted aged 1 week with vomiting. *Clinical diagnosis:* Mongolism with duodenal atresia. Died on tenth day. *Necropsy:* Mongolism; duodenal atresia just below ampulla; partial patency of foramen ovale.

Case 4.—A male child born six weeks before term after surgical induction for hydramnios. Eighth child; mother aged 36. Admitted aged 4 days with vomiting from birth. *Clinical diagnosis:* Mongolism; prematurity and duodenal atresia. Death occurred on the sixth day. *Necropsy:* Mongolism; duodenal atresia immediately above ampulla; interventricular septal defect; cerebellum disproportionately small; undescended left testicle.

Case 5.—A male child, third in family. Admitted on day of birth with progressive jaundice. Rh incompatibility; direct Coombs's test positive. Typical mongol. *Clinical diagnosis:* Haemolytic disease of the newborn with mongolism. Death took place on second day. *Necropsy:* Mongolism; severe duodenal stenosis 1 cm. above the papilla; cerebral kernicterus; erythroblastosis foetalis; Meckel's diverticulum.

Case 6.—A first-born female child, two weeks premature; white asphyxia at birth following difficult forceps delivery. Mother aged 35. Admitted aged 3 days with vomiting from birth and passage of only mucus per rectum. *Clinical diagnosis:* Intestinal obstruction. *Operation:* Duodeno-jejunostomy for atresia at duodeno-jejunal flexure; lack of mesenteric attachment of ascending colon noted. Discharged home at 1 month of age after a stormy convalescence. Recognized as a typical mongol when seen in an out-patient clinic at 5 months of age.

Case 7.—A male child, third in family. Mother aged 36; suffered from hydramnios during pregnancy. Admitted aged 7 days because of persistent vomiting. *Clinical diagnosis:* Intestinal obstruction. *Operation:* Gastro-jejunostomy for duodenal atresia. Died shortly after operation. *Necropsy:* Mongolism; complete membranous occlusion of duodenum immediately distal to ampulla; extensive peritoneal haemorrhage; small cerebellum; undescended left testicle.

Case 8.—A female child five weeks premature, fifth of family. Mother aged 40; hydramnios during pregnancy. Admitted on third day with vomiting from birth. *Clinical diagnosis:* Atresia of duodenum. *Operation:* Duodeno-jejunostomy for atresia of proximal 4 in. (10 cm.) of jejunum. Died shortly afterwards. *Necropsy:* Mongolism; duodenal atresia immediately distal to papilla; multiple atresias of proximal jejunum; small intestine much shorter than normal; universal mesentery; cerebellum disproportionately small; partial patency of foramen ovale; failure of lobation of left lung.

Case 9.—A first-born full-term female child. Mother aged 25; hydramnios during pregnancy. Infant suffered asphyxia at birth. Admitted aged 5 days with vomiting, cyanotic attacks, and purpura. *Clinical diagnosis:* Duodenal atresia and possible mongolism. *Operation:* Peritoneal bands divided. Death on eighth day with oedema and cardiac failure. *Necropsy:* Extensive peritoneal haemorrhage; duodenal atresia immediately above the papilla; mongolism, small cerebellum; large auricular septal defect (septum secundum); pulmonary oedema.

Case 10.—A male child, eighth in family. Maternal age 39; hydramnios during pregnancy. Following severe birth asphyxia the infant began to regurgitate brown fluid. Admitted aged 5 days. *Clinical diagnosis:* Mongolism and duodenal atresia. *Operation:* Gastro-jejunostomy. Deterioration after tenth day with diarrhoea; death at 3 weeks of age. *Necropsy:* Mongolism; severe duodenal stenosis immediately proximal to the ampulla; universal mesentery; small brain; aberrant right subclavian artery; umbilical sepsis; oral thrush.

Discussion

Textbooks of surgery and paediatrics do not in general refer to this association, which in our experience has occurred with remarkable frequency, nor is it mentioned in the monographs of Benda (1947) and Engler (1949) on mongolism. In a survey of published cases of duodenal obstruction in the newborn Forshall (1947) found only five instances in which associated mongolism had been observed. More recently, however, Lanman (1949), in Boston, reported that, of 17 children with duodenal

atresia successfully treated by operation, 4 were subsequently found to be mongols, while Grove and Rasmussen (1950) found 3 mongols among 11 cases of duodenal atresia or stenosis.

One of us (L.L.R.W.) recently observed mongolism in three successive infants with duodenal atresia at necropsy, in Cardiff, and from personal communications we have learned that Miss I. Forshall, in Liverpool, has seen four cases, and Miss V. Smallpeice, at Oxford, two cases.

From our observations there would appear to be a high incidence of mongolism in infants suffering from intrinsic malformations of the duodenum, the overall frequency in 25 years being approximately one in three. It is remarkable, however, that during 1951, after our interest had been drawn to the association, all five cases of duodenal atresia or stenosis admitted to Great Ormond Street have been found to be mongols; in two of these the latter condition was not recognized until post-mortem examination. Our recent experience suggests that the frequency of associated mongolism may be even higher than one in three.

A possible explanation of the paucity of recorded instances is that most uncomplicated cases of mongolism do not come under medical observation until there is obvious retardation of mental progress, at the end of infancy or later. On the other hand, most cases of duodenal atresia or stenosis die in the neonatal period at a time when the classical appearances of mongolism, though present, are not conspicuous.

The features of mongolism in newborn infants are perhaps not as widely appreciated as they might be (Carter and MacCarthy, 1951). On clinical inspection the immediate general impression is that the baby has an odd appearance. Only a careful systematic examination will elicit the presence of some of the signs of mongolism.

The head is usually rounded, and on palpation of the sagittal suture a third fontanelle may be found. The facial contour is square; the oblique palpebral fissures are small and measure less than the interocular distance; medial epicanthic folds are usually present; the nasal bridge is depressed; the ears are poorly formed and have a crumpled appearance; the tongue tends to protrude. Fingers are somewhat short and the little finger may be incurved owing to a short middle phalanx; a single transverse palmar crease is often present; the axial triradius is in an abnormal position (Penrose, 1949). A high maternal age affords further circumstantial evidence.

At post-mortem examination the most characteristic internal finding is a disproportionately small cerebellum and brain stem; associated malformations, notably cardiac septal defects, may be encountered.

It must be emphasized that no one feature is peculiar to mongolism, nor is any sign of invariable occurrence; it is the presence of a majority of these signs, however, which enables one to make the diagnosis with reasonable certainty, even in the newborn.

In view of our observations it seems important to seek evidence of mongolism in all infants with suspected duodenal obstruction, since such finding may influence the decision to operate.

Summary

In a consecutive series of 32 infants with congenital atresia or stenosis of the duodenum a high incidence of mongolism was observed.

The frequency of this association has not been generally appreciated, presumably because most children with duodenal atresia or stenosis die during the neonatal period, when mongolism is apt to be overlooked. The features of the newborn mongol are therefore reiterated. It is felt that the early recognition of mongolism in a newborn child with suspected duodenal obstruction may be of practical importance in the management of the case.

Acknowledgments are due to the clinical staff of the Hospital for Sick Children for permission to use their case records. We are also indebted to Miss I. Forshall and Miss V. Smallpeice for their personal communications.

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ACUTE INFECTIOUS LYMPHOCYTOSIS

REPORT ON A GROUP OF CASES IN A DAY NURSERY

BY

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Acute infectious lymphocytosis was first described as a specific disease by Carl H. Smith, of New York, in 1941. It chiefly affects children below the age of 10 years, and is known to occur sporadically and also in small epidemics, particularly in institutions and among members of the same family. The literature and features of the condition were fully reviewed by Smith himself in 1947. Most of the case reports have come from North America, and the largest recorded outbreak there involved 86 persons in an institution for mentally defective and epileptic patients (Barnes *et al.*, 1949). During the last few years instances of the disease have also been reported increasingly in Europe. Thus the condition has been encountered in Finland (Klemola and Hamarinen, 1947), in Switzerland (Gsell, 1947; Landolt, 1947; Martens, 1948), in France (Debré *et al.*, 1948; Lamy, 1948; Bernard *et al.*, 1948), and in Germany (Recknagel, 1948; Koch, 1949; Heni and Zeh, 1949), as well as in Austria, Czechoslovakia, Greece, the Netherlands, Sweden, and Spain.

In this country, Kilham and Steigman (1942) first pointed out certain similarities to infectious lymphocytosis in three children whose blood showed an increase in the number of small lymphocytes and gave a negative Paul–Bunnell reaction. Later, Steigman (1946) briefly described a small outbreak affecting six children in a village in Southern England in 1942. Isolated instances of the condition in the East End of London have been reported from this hospital (Sita-Lumsden, 1947) and from Mile End Hospital (Dolphin and Popham, 1950). An account of three cases was also published in Northern Ireland (McCollum, 1949).

Six cases which appeared to originate in a day nursery in East London are described below. The first three were encountered in hospital practice.

Case 1

A female infant aged 1 year and 4 months was first sent to the out-patient department of the London Hospital from a local day nursery on August 4, 1950. She had always had a tendency to pass offensive loose stools with mucus, but for the previous fortnight this had been worse and she had had about seven motions daily. She was, however, still eating well and had not vomited. Her development and previous health had been normal apart from a severe attack of whooping-cough and intermittent right otorrhoea. She was the youngest of four children, and the mother reported that the others, who were all boys, were also liable to pass loose stools. The eldest had had diarrhoea for three weeks about three months previously, and the second had had it for one week a fortnight previously.

On examination the child looked healthy, and her temperature was normal. The right eardrum was hyperaemic and dull; otherwise there were no abnormal signs. The lymph nodes and spleen were not enlarged. A rectal swab revealed nothing abnormal in a film or on culture.

On treatment with dietary restriction and a kaolin mixture the stools diminished in number but remained loose and offensive. A week after her first attendance she had lost 2½ oz. (71 g.) in weight and appeared paler. The blood then showed a haemoglobin concentration of 74%* and a white-cell count of 79,400 per c.mm., with 95% lymphocytes, which were normal in appearance.

On the following day, August 12, she was admitted to hospital. She was now fretful and had a temperature of 102° F. (38.9° C.). The tonsillar lymph nodes were palpable. The fauces were slightly congested and showed some post-nasal mucous discharge. Both eardrums were hyperaemic. Otherwise she was normal.

The stools were found to contain many flagellates and cysts of *Giardia lamblia*. No pathogenic organisms were grown on repeated culture of stools and rectal swabs. Throat swabs and urine tests showed nothing abnormal, the erythrocyte sedimentation rate (Wintrobe) was 12 mm. in one hour, and a tuberculin jelly test proved negative.

Treatment consisted of intramuscular penicillin (100,000 units twice daily) and 0.5% ephedrine nose drops. The temperature declined for the first two days, then rose to 103.4° F. (39.7° C.), while a severe aphthous stomatitis developed. This appeared clinically characteristic of a herpetic infection; numerous small ulcers developed on the tip of the tongue and on the buccal mucous membrane, and vesicles spread on to the lips and skin outside the mouth.

The blood count on August 14 showed: haemoglobin, 65%; white cells, 80,000 per c.mm., with 91% lymphocytes. On August 19 blood was taken for Paul–Bunnell and herpes complement-fixation tests; both were negative in all dilutions. The fever appeared unaffected by penicillin, but the temperature, though swinging, declined gradually and reached normal after 12 days.

On August 22 the white-cell count had fallen to 24,500, with 72% lymphocytes. A course of mepacrine (0.05 g. twice daily for four days) was then given for the giardiasis, as well as a ferrous sulphate mixture for the anaemia. Further progress was uneventful, and the child's condition was fairly satisfactory. Three further stool tests demonstrated disappearance of the *G. lamblia* parasites.

On August 31 the blood count showed: haemoglobin, 65%; red cells, 4,060,000 per c.mm.; white cells, 11,400, with 62% lymphocytes. By September 11 the haemoglobin concentration had risen to 76%, while the white-cell count had fallen to 7,900 per c.mm., with 52% lymphocytes and 10% eosinophils. On September 27 the leucocyte count was normal (see Table I).

The complement-fixation test for herpes was repeated on August 31 and again on November 1, but remained negative. The Paul–Bunnell test was also negative again on the latter date.

Case 2

A boy aged 2 years and 5 months, the youngest brother of Case 1, also attended the nursery. He first came to the out-patient department on August 23, 1950. Like his sister, he had passed loose stools intermittently before. He had also been treated for enteritis in a fever hospital in April, 1949. He now had a cough of one week's duration, and during this time had had up to five watery motions daily.

On examination he looked healthy, and his temperature was normal. Except for the presence of post-nasal mucopus in the pharynx and slight prominence of the abdomen there were no abnormal signs. A blood count showed 79,400 white cells per c.mm., of which 97% were lymphocytes; these were normal in appearance. A stool specimen contained *G. lamblia* cysts and flagellates. A course of mepacrine, 0.05 g. three times daily for five days, was prescribed, and the boy was removed from the nursery.

A week later, on August 30, the mother reported that he still passed four or five loose motions without mucus every

*The alkaline haematin method of estimation with photoelectric colorimetry was used throughout; 100% = 14.8 g. of haemoglobin per 100 ml.

TABLE I.—*White Blood Cell and Differential Counts of Affected Children*

Case No.	Date (1950)	Total Count per c.mm.	Lymphocytes % (total per c.mm.)	Eosinophils % (total per c.mm.)	Neutrophils %	Monocytes %	Basophils %
1	Aug. 11	79,400	95 (75,430)	1 (794)	4	—	—
	,, 14	80,000	91 (72,800)	—	9	—	—
	,, 22	24,500	72 (17,640)	—	24	4	—
	,, 31	11,400	62 (7,068)	—	35	3	—
	Sept. 11	7,900	52 (4,108)	10 (790)	33	5	—
	,, 27	5,200	58 (3,016)	1 (52)	36	5	—
2	Aug. 23	79,400	97 (77,018)	—	3	—	—
	,, 30	61,000	91 (55,510)	2 (1,220)	7	—	—
	Sept. 6	19,600	69 (13,524)	8 (1,568)	21	2	—
	,, 13	10,200	49 (4,998)	2 (204)	47	2	—
3	Aug. 30	40,000	88 (35,200)	—	11	1	—
	Oct. 20	10,400	74 (7,696)	4 (416)	22	—	—
4	Sept. 22	42,700	91 (38,857)	3 (1,281)	6	—	—
	,, 28	31,800	85 (27,030)	4 (1,272)	9	2	—
	Oct. 19	10,100	42 (4,242)	5 (505)	47	6	—
	Dec. 11	10,000	20 (2,000)	3 (300)	75	2	—
5	Sept. 19	14,800	79 (11,692)	—	21	—	—
	Oct. 5	15,300	78 (11,934)	2 (306)	18	2	—
	,, 19	23,800	78 (18,564)	4 (952)	18	—	—
	,, 26	11,000	66 (7,260)	5 (550)	26	2	1
6	Oct. 12	50,400	84 (42,336)	5 (2,520)	11	—	—
	,, 20	40,800	70 (28,560)	4 (1,632)	23	3	—
	Nov. 7	5,700	28 (1,596)	10 (570)	58	4	—

day. He had also developed a cold, but was eating well. There were no new signs except those of coryza. The blood count showed: haemoglobin, 86%; leucocytes, 61,000 per c.mm., with 91% lymphocytes and 2% eosinophils. A specimen of stool and a rectal swab revealed no abnormality on film or culture.

During the following week the motions became normal again and the boy began to gain weight. On September 6 the haemoglobin concentration had fallen to 74% and the white-cell count to 19,600 per c.mm., of which 69% were lymphocytes and 8% eosinophils. The stool was again normal on film and culture. A week later the white cells had diminished further to 10,200, and the differential count was normal (see Table I). A Paul–Bunnell test on October 11 showed heterophil antibodies within normal limits (up to a titre of 1:10).

The two elder brothers were also examined. The first was a schoolboy 5½ years old. He also had occasional diarrhoea, but repeated stool examination showed nothing pathological, and his blood count was normal on two occasions. The second brother, aged 3½ years, attended the same day nursery as the two younger children. He was seen on August 23, when he had diarrhoea and signs of bronchiolitis; he was found to pass *G. lamblia* flagellates and cysts in his stool, and his white blood count was 14,300 per c.mm., of which 55% were polymorphonuclear neutrophils and only 42% lymphocytes. He was given a course of mepacrine, 0.05 g. three times daily for five days, and the diarrhoea subsided after a week. Three further stool tests were then negative for *G. lamblia*. On September 16 he was quite well; the blood count showed a haemoglobin content of 74% and 19,800 leucocytes per c.mm., with 53% lymphocytes and 10% eosinophils. Subsequently the white-cell count fell to normal levels. In October he had some loose stools again, and a specimen once more revealed a few *G. lamblia* flagellates.

The mother of these children had no diarrhoea. Her blood count and stool examination were normal.

Case 3

A baby girl attended the same day nursery as the children described previously. In June, 1949, she had had bacillary dysentery of the Flexner type and had been treated with sulphaguanidine. After that she continued to pass five or six relaxed stools daily, and because of this she had been seen at the out-patient department in November, 1949, when she was 17 months old. Stool examination then revealed the presence of many cysts of *G. lamblia*. She was given mepacrine, 0.05 g. twice daily for 10 days. Subsequently her motions were normal until February, 1950, when she started having intermittent diarrhoea again. Stool and rectal swab examinations were normal in February and March, but on May 5 many *G. lamblia* cysts were again present in the stool. After another course of mepacrine, 0.05 g. twice daily for five days, the stools became normal. In August she was brought up again because of mild diarrhoea. Two rectal swabs and two stool tests showed nothing abnormal, but a blood count on August 30 demonstrated a haemoglobin concentration of 79% and a leucocytosis of 40,000 cells per c.mm. with 88% lymphocytes. At that time she had coryza and a cough, but the fauces appeared normal, and lymph nodes and spleen were not enlarged. Unfortunately, she then ceased to attend the hospital and was not brought to the nursery again until mid-October. On October 20 she was examined there and appeared healthy. The jugular lymph nodes were palpable, the fauces were slightly injected, and the abdomen was rather prominent. The white-cell count was now 10,400 per c.mm., with 74% lymphocytes.

Investigations at the Nursery

Thus *G. lamblia* infestation was known to be present in four, and lymphocytosis, presumably of the acute infectious type, in at least three children attending this particular nursery. It was decided to make further investigations there in order to determine the incidence of the two conditions.

The nursery is a fairly spacious and modern building in one of the back streets of Whitechapel. At the time of the inquiry there were 53 children in daily attendance from Monday to Friday.

It would have been most interesting to carry out weekly clinical examinations, blood counts, and stool tests on all the children and their adult attendants in the nursery. But, as time and laboratory facilities were limited, it was decided to deal with not more than six persons on any one day and to go through the whole nursery population in that manner. Blood counts and stool tests were only repeated in those in whom clinical or laboratory findings suggested some abnormality.

Between September 11 and October 26 all the children at the nursery were examined personally, and at least one blood count and stool test were performed on each of them. Blood samples were also taken from the 22 adults who were working there; only eight stools were obtained from these. It may be stated at once that nothing abnormal was found in the individual tests on the adults.

Nine children were shown to pass *G. lamblia* cysts in their stools. With the members of the family of Cases 1 and 2 this adds up to 12 infested children out of 53. The real incidence may be assumed to have been considerably higher, as it is well known that *G. lamblia* may be found only after repeated testing of stools and that one examination per case will discover only from one-third to one-half of the actual number of infections (see Boeck, 1927). Moreover, the faeces were examined by inspection of wet films in saline and not by concentration methods.

The blood counts revealed only one further definite and one probable case of lymphocytosis. Adding the previous patients, this gives a total of 5 out of 53 children in the nursery.

Case 4

A boy aged 3 years had been perfectly well without complaints of any kind. On examination on September 22 he appeared healthy, and his rectal temperature was normal. There were no abnormal signs; his lymph nodes and spleen were not enlarged. Surprisingly, his white-cell count was 42,700 per c.mm., of which 91% were normal lymphocytes and 3% eosinophils. His stool on that day contained many cysts of *G. lamblia*.

On September 28 the leucocytosis was reduced to 31,800 per c.mm., with 85% lymphocytes and 4% eosinophils. After another three weeks the count had returned to normal levels at 10,100 per c.mm., of which only 42% were lymphocytes, but still 5% eosinophils. A Paul–Bunnell test was negative. Like the other children with giardiasis he was given a course of mepacrine, and three subsequent stools were free of parasites. In December he was admitted to hospital suffering from concussion and fracture of the left tibia after an accident. His blood count then showed a haemoglobin concentration of 70%, white cells 10,000, with only 20% lymphocytes and 3% eosinophils (see Table I).

Case 5

A girl aged 3 years and 4 months, who had been free of symptoms, was first examined on September 19, and appeared healthy. Her rectal temperature was normal. The only abnormal signs were the presence of post-nasal muco-

pus and of palpable jugular and right posterior cervical lymph nodes. Her blood count showed 14,800 white cells with 79% lymphocytes. Her stool specimen on October 2 contained many cysts of *G. lamblia*.

She remained well and was given a course of mepacrine. As the initial lymphocyte count was high, further samples of blood were examined at intervals. On October 5 this showed 15,300 leucocytes per c.mm., of which 78% were lymphocytes. By October 19 the total count had risen to 23,800, still with 78% lymphocytes. A week later it had fallen to 11,000, with 66% lymphocytes. The stool was free of parasites on October 24.

This girl thus had an absolute lymphocytosis reaching three times the maximal normal value, which according to Smith (1941) should be about 6,000 lymphocytes per c.mm. at this age. It may be argued that she had a non-specific lymphocytosis due to upper respiratory tract infection, but against this it should be pointed out that the increase in the number of lymphocytes was more marked than in that condition (see Smith, 1941) and ceased fairly suddenly.

The other 47 children showed no gross clinical abnormality, but some evidence of upper respiratory tract infection was found in no fewer than 17. The leucocyte counts varied from 5,200 to 21,100 per c.mm. with an average of 11,200, and are arranged according to age groups in Table II, together with those of the adults. Whenever a child had more than one count, only the first has here been used for calculation, in order to avoid weighting the averages in favour of high values.

TABLE II.—*Other White-cell and Lymphocyte Counts in the Nursery*

Age	No. of Persons	Average Total White-cell Count per c.mm.	Average Total Lymphocyte Count per c.mm.	Corresponding Lymphocyte Percentage
3 months–1 year	4	12,875	8,686	67·5
1–2 years ..	12	12,008	7,297	60·8
2–3	15	10,513	6,253	59·5
3–4	9	10,700	5,757	53·8
4–5	7	10,971	5,377	49·0
All children ..	47	11,200	6,523	58·2
Adults	22	9,014	3,402	37·7

Kato (1935) found in a large series of normal American children that the average white-cell count gradually fell from 11,000 per c.mm. at the age of 3 months to about 7,500 at 9 years, and that the average absolute lymphocyte count declined from over 6,000 in the second month of life to the adult level of 2,500 at 15 years, being equalled by the granulocyte count at 4,000 per c.mm. at the age of 4 years. Again, Smith (1941) states that the *maximal* normal absolute number of lymphocytes drops from approximately 7,000 per c.mm. at 1 or 2 years of age to 6,000 at 3 or 4 years, and finally to 5,000 at puberty, while the *maximal* normal lymphocyte percentage is about 60 between 6 months and 2 years of age and 50 by the end of the sixth year.

A variety of normal values are given in textbooks, but at least in comparison with these American data the average total white-cell and absolute and relative lymphocyte counts will be seen to have been high in the nursery. Therefore it would seem quite likely that there were some more cases of infectious lymphocytosis with only slight blood changes. However, many mild infections will cause a slight absolute lymphocytosis in children, and thus I have thought it best not to label any case as acute infectious lymphocytosis unless the absolute lymphocyte count exceeded twice Smith's maximal normal value for the age concerned. Only the patients described so far satisfied this criterion.

I thought it would be interesting to investigate the family of Case 4 in order to see whether any other members had lymphocytosis or giardiasis. This boy had an elder sister and a 6-year-old brother who were schoolchildren. The mother was asked to bring them to the nursery to be examined. She herself had a normal white cell and differential count; the brother's counts were also normal on three occasions and his stool was free of parasites; but the sister (Case 6) had lymphocytosis.

Case 6

A girl aged 7 years was first seen on October 6. She had had intermittent frontal headaches for a few months, and her appetite had been only moderately good. She had also complained of toothache and right earache for one week, and had had several carious teeth extracted on the morning of the day when I first saw her.

On examination she was pallid but well nourished. Her tonsils and jugular lymph nodes were slightly enlarged. Otherwise, apart from the tooth sockets containing fresh blood clots, there were no abnormal findings. The first blood count was performed on October 12. It showed 50,400 white cells per c.mm., with 84% lymphocytes, which were normal in appearance. On October 20 the white-cell count had fallen to 40,800, of which 70% were lymphocytes and 4% eosinophils. On the same day the Paul–Bunnell test was negative. The girl was not seen again until November 7, when the white-cell count had returned to normal; her stool then contained no parasites. She was well during the whole of this period. One further stool test proved normal.

Discussion

These six cases satisfy all the criteria of acute infectious lymphocytosis (Smith, 1941)—namely, marked leucocytosis with absolute lymphocytosis; benign clinical course; absence of splenomegaly and of significant lymphadenopathy; negative Paul-Bunnell test; and no manifestations of infectious mononucleosis or of leukaemia—lymphocytes of small normal mature type.

Epidemiology.—As regards the epidemiology of the disease, the present experience confirms that its infectivity generally tends to be low. Reyersbach and Lenert (1941) encountered only 16 cases during six months in an institution housing 108 children; I found only five on mostly single blood estimations in the course of about two and a half months in a day nursery with 53 children. However, in some reports the condition has affected a higher proportion of children in more epidemic form (Finucane and Philips, 1944; Barnes *et al.*, 1949). It is also possible that some of the contacts may be infected without developing fully characteristic blood changes; this may have happened, for instance, in the second brother of Case 1. The incidence among members of the same family has been observed before (Smith, 1944; Moyer and Fisher, 1950) and is well illustrated by the present cases.

Incubation Period.—This has been estimated as being between 12 and 21 days (Smith, 1944); in one of the cases of Barnes *et al.* (1949) it appeared to be 16 days. It may be assumed that my Case 6 acquired the infection from her brother (Case 4), who attended the nursery, and it is interesting that their lymphocyte counts, while falling, reached roughly similar levels at an interval of just over three weeks. It is less safe to assume that Case

2 was infected by his sister (Case 1), as both attended the nursery; in these, the corresponding interval was just below two weeks. If these intervals are any guide to the incubation period, it would agree fairly well with the suggestions made by the observers quoted above.

Symptomatology.—The symptomatology in these patients was similar to that of previously recorded cases. In a considerable proportion there may be no symptoms at all, and the condition may be discovered only on blood examination; this occurred in two of my six cases. Of the possible clinical features, fever is said to be present in some cases at the onset. It was found in only the first of these patients, but here it was severe, as in Duncan's (1943) case. Abdominal symptoms are not infrequent and may even simulate an acute surgical condition; the commonest complaint is diarrhoea, which may occur in mildly epidemic form (Peterman *et al.*, 1949), and this was present in three out of the six cases described here. Perhaps it is more likely to occur in those with previously abnormal bowel function, for in all three patients with this symptom there was a past history of loose stools, and *G. lamblia* infestation may have played a part. Mild upper respiratory infection is common in this disease: some evidence of it was found in five of these six patients. Symptoms or signs of meningeal irritation have been reported in occasional cases, but were not evident in the present ones. As regards skin manifestations, it is of interest that Smith (1944) observed a herpetic eruption on the face of a child at the onset of the disease. In my first case the aphthous stomatitis and vesicles on the lips strongly resembled herpetic lesions; yet the complement-fixation test for herpes was repeatedly negative. One wonders whether acute infectious lymphocytosis should be remembered as a possible cause of apparent herpetic eruptions and also whether a virus might be cultured from these vesicles in lymphocytosis.

Haematological Findings.—These correspond to those observed elsewhere. In five of my six cases the maximal total white-cell counts exceeded 40,000 per c.mm. The highest proportion of lymphocytes varied between 79 and 97%. The lymphocytes were normal in size and structure, and thus differed from those usually found in glandular fever. The total duration of the abnormal lymphocyte levels could not be estimated, as no observations were made while these were rising from normal. The periods of fall lasted two to four weeks, and this agrees approximately with Finucane and Philips's (1944) observation that the leucocytosis lasted from two and a half to seven weeks, with an average probable duration of about five weeks.

An absolute eosinophilia has been observed by several previous authors (Finucane and Philips, 1944; Landolt, 1947; Barnes *et al.*, 1949). The figure of 400 per c.mm., which is often given as the upper limit of normal (Whitby and Britton, 1950), was exceeded in all my six cases, and at least five of them had more than 790. In two of them the maximum eosinophilia occurred after the peak of the lymphocytosis. Monocytes were often absent at the height of the disease and reappeared towards the end as they do in other acute infections. The platelets were always plentiful in the films.

Differential Diagnosis.—In arriving at a diagnosis several diseases had to be considered. Glandular fever first came to mind, but there was no splenomegaly and little lymph-node enlargement, which was confined to the neck; also, the leucocyte count showed a greater increase, the lymphocytes were normal in type, and the Paul–Bunnell test was negative in four cases. Leukaemia was ruled out by the benign course, and by the absence of lymphadenopathy, of abnormal blood cells, and of thrombocytopenia. There was no clinical evidence to support the possibility of whooping-cough. Chronic non-specific lymphocytosis of the type which may accompany and follow upper respiratory or other infections was unlikely to be the cause as the leucocyte response was too marked and short in duration.

Possible Relationship to G. lamblia Infestation.—Finally, this question has to be discussed. The total incidence of giardiasis in 12 out of the 53 children at the nursery, as determined by mostly single stool tests, is probably within the usual limits, for Boeck (1927) found that the incidence in children reported in the literature varied from 14 to 40%, and it is known to be even higher in residential institutions (Brown, 1948). There is still no agreement concerning the pathogenicity of these parasites, but they can probably be responsible for malabsorption (Véghelyi, 1940) and may sometimes cause enteritis (Miller, 1926; Ormiston *et al.*, 1942). Among my 12 cases of known *G. lamblia* infestation it was noteworthy that 7 had a history of diarrhoea within the last month, whereas only 5 out of 40 children without parasites in their stools had had this experience. However, it must also be remembered that diarrhoea by itself may wash *G. lamblia* flagellates down from the duodenum and jejunum, which are their habitat. It is interesting that the 12 children in this series who are known to have harboured the parasites included five out of the six cases with lymphocytosis, and that at least four of these six were passing *G. lamblia* at the time of the disease; but there is no proof of any definite association, and this will have to be a matter for future investigation.

Summary

Six cases of acute infectious lymphocytosis are recorded. The patients were children whose ages ranged from 16 months to 7 years. Five of these attended a day nursery in the East End of London, and the sixth was the elder sister of one of the others.

The constitutional symptoms were fairly severe in the youngest child, who had marked fever and aphthous stomatitis; the latter resembled a herpetic infection clinically, but was not associated with a positive complement-fixation reaction to herpes simplex. The other cases were mild, and at least two patients had no symptoms attributable to the condition.

Four of the six children were found to pass *G. lamblia* flagellates or cysts in their stools, and a fifth had received two courses of treatment for this infestation during the previous year.

Three of the patients attended the out-patient department of a hospital because of diarrhoea. The others were found on the basis of mostly single blood counts performed on the remaining 50 children attending the nursery and on 23 adult and two child contacts in the course of about six weeks. Single stool tests, performed simultaneously, showed that a total of 12 out of the 53 nursery children harboured *G. lamblia* parasites.

The epidemiology, clinical features, blood changes, and differential diagnosis of acute infectious lymphocytosis are briefly discussed in relation to the cases described.

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TUBERCULOUS MENINGITIS

TREATMENT WITH STREPTOMYCIN AND PARA-AMINOSALICYLIC ACID

BY

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An apparent cure, without sequelae, can be expected in 50% of cases of tuberculous meningitis treated by streptomycin, and, provided skilful treatment is given early in the disease, a higher percentage can make a complete recovery. In an attempt to increase the recovery rate by using *para*-aminosalicylic acid (P.A.S.) in combination with streptomycin 35 cases of tuberculous meningitis were treated and reviewed at Castle Hill Hospital.

On admission all cases were classified as: (1) Early case (E)—fully conscious patient, with no focal signs, slight nuchal rigidity but with abnormal cerebrospinal fluid. (2) Middle case (M)—fully conscious, but sometimes drowsy and lethargic, with nuchal rigidity and focal signs. (3) Advanced case (A)—unconscious or deeply stuporous patients.

The diagnosis was confirmed by isolation of the tubercle bacillus from the cerebrospinal fluid in 30 cases. The five in which tubercle bacilli were absent showed other specific signs and symptoms of the disease.

The results of treatment were assessed after a minimum survival period of one year from the date of admission, and cases were observed for up to 30 months.

Treatment

All cases were given a six-months' course of intramuscular and intrathecal streptomycin combined with oral P.A.S. The daily dose of intramuscular streptomycin was 1 g. and was given to all patients in two twelve-hourly doses of 0.5 g. The daily dose of intrathecal streptomycin was 100 mg. for patients of 5 years and over, and 50 mg. for those under 5 years. Oral P.A.S. was given in gradually increasing dosage as follows: 3 g. for patients 12 years or over, 1.5 g. for those 5–11 years, and 0.75 g. for those 1–4 years—1 dose daily for three days, then 2, 3, 4, 5, and 6 doses each for three days, so that at the end of 18 days each patient was receiving six doses a day at intervals of two-and-a-half hours, from 9 a.m. to 9.30 p.m. The tendency to nausea and vomiting was much reduced if the patient ate something before a dose—for example, a few biscuits and milk. An alkaline mixture given before a dose may help in preventing nausea, and a chalk-and-opium mixture may be given for the treatment of diarrhoea. However, with the above dosage these symptoms were rarely met with. P.A.S. was given continuously throughout the patients' stay in hospital in the recommended dosage. On discharge it was continued as a bacteriostatic agent at a reduced dosage throughout the period of observation.

Treatment was given for six days a week, Sunday being a complete rest period. All patients were kept in bed for the six-months course of streptomycin treatment. A radiograph of the lungs was taken and full chemical and bacteriological examinations of the cerebrospinal fluid (C.S.F.) were made monthly. Patients were not allowed up until the C.S.F. was normal, and they were kept in hospital for at least one year.

Diagnosis

In the known tuberculous child with obscure symptoms, spread to the meninges must always be considered; the incidence of meningitis is highest in the first three months after the development of the primary lung lesion. Children exposed to tuberculosis at home must be kept under observation for the beginning of a primary lung lesion and for subsequent spread to the nervous system. The signs and symptoms of tuberculous meningitis are varied, but most cases conform to a general pattern. Rarely the onset is sudden, with focal signs in the nervous system such as convulsions, cranial nerve paralysis, and limb paralyses. More often the meningitis begins insidiously, with symptoms which may at first mimic minor ailments.

The disease tends to be most treacherous in infancy and early childhood, with a more vague onset and more rapid progress than is usual in the older patient. In older children listlessness and irritability may be the first symptoms: an otherwise good-natured and happy child loses interest in his toys and quarrels with his playmates. The parent may remark that he is easily tired and that he falls asleep in a chair or at mealtimes. Headache is a common complaint of older children in the early stage, and vomiting may occur.

History of Contact.—A definite history of contact with diagnosed tuberculosis in the home was found in 14 of the 35 cases.

Mantoux Test.—This test is a highly significant aid to diagnosis, particularly in young children. Reliance should not be placed on the tuberculin patch or jelly test performed during the course of meningitis, because the allergic response to tuberculin is commonly reduced in these cases, so that a negative result is obtained. A properly performed Mantoux test, using fresh material and a 1 in 100 solution if the 1 in 1,000 is negative, is positive in over 90% of cases. The Mantoux test was performed in all cases. The reactions are shown in Table I.

TABLE I

	E Cases	M Cases	A Cases	Total
Positive at 1 in 10,000 ..	2	5	2	9
,, ,, 1 in 1,000 ..	0	8	17	25
,, ,, 1 in 100 ..	0	0	1	1
Negative in all three dilutions	0	0	0	0

Radiography.—Routine chest radiography proved another valuable aid. Definite abnormalities in the chest *x*-ray film were seen in 23 of the 35 cases. (Two patients died before radiographs could be taken.) They comprised (*a*) a primary complex (usually hilar adenitis with a pulmonary focus) in 14 cases; (*b*) miliary disease of the lungs in seven cases; and (*c*) phthisis present in two adults. In the remaining 10 cases no abnormality was seen.

C.S.F. Examination.—The general appearance of the C.S.F., cell count, protein content, chlorides, and sugar were estimated monthly along with direct examination for tubercle bacilli and culture on Lowenstein's medium. For the initial diagnosis as many as 12 daily C.S.F. examinations were done. If a Mantoux-positive case with no tubercle bacilli on direct examination showed a lymphocytosis with increased protein and lowered sugar and chloride content on two occasions, treatment was begun without further delay. These cases were nursed in isolation until their C.S.F. cultures showed tubercle bacilli; they were then transferred to the tuberculous meningitis ward. Cases of tuberculous meningitis with positive sputum were nursed in isolation during their 12 months' stay in hospital. Thirty cases showed tubercle bacilli in the C.S.F. Of the five remaining cases, one was proved post mortem to have tuberculous meningitis and four were Mantoux-positive, and their C.S.F. showed a lymphocytosis with increased protein and lowered sugar and chlorides on more than two occasions. Other causes of a lymphocytosis in the C.S.F. which require to be considered in the differential diagnosis are: polio-encephalitis and poliomyelitis; benign lymphocytic choriomeningitis; glandular fever; mumps encephalitis; spirochaetal infections (syphilis, leptospiral diseases, relapsing fever); infective hepatitis; atypical pneumonia; herpes zoster; psittacosis; trypanosomiasis; and yeast meningitis.

Results

Of the 35 patients treated, 28 survived and 7 died. Of the 28 survivors 26 have normal C.S.F.; 19 are clinically fit and well, and of the remaining nine three are fit and well except for partial deafness, audiograms showing loss of hearing of 10–40 decibels. These cases are being fitted with hearing-aids and their progress is under observation. The six remaining cases showed the following features.

Case 10.—A woman, aged 20, on admission was six months pregnant, was comatose, and had right hemiplegia. She was given combined treatment, and caesarean section was done at the 38th week of pregnancy. The baby was born alive, but died after 48 hours. At the end of 581 days the patient was fit and well and showed only slight paresis of the right leg; she could walk and do her ordinary housework with the aid of a calliper splint on that leg. The C.S.F. on the 581st day was normal.

Case 13.—A boy, aged 3, on admission had tuberculous meningitis, miliary tuberculosis of lungs, and tuberculosis of the right ankle, which broke down and discharged freely. On the 850th day he was fit and well, but the C.S.F. showed a lowered sugar content. He wears a calliper splint for the right ankle condition, which has healed.

Case 15.—A boy aged 1 year. On the 584th day of observation he was well nourished and the C.S.F. was normal, but he was mentally retarded. Since discharge from hospital his guardian states that he has greatly improved and is now able to walk, but he will require psychometric assessment at a later date.

Case 25.—A boy, aged 23 months, was comatose and blind on admission. On the 639th day of observation he could see, walk, and run, and was attempting to talk. He was also partially deaf and mentally retarded, and will require psychometric assessment at a later date.

Case 28.—A girl aged 14 completed a full course of treatment and was discharged home after one year in hospital. Six months later she was readmitted with miliary tuberculosis of the lungs and given a three-months course of 1 g. daily of dihydrostreptomycin and P.A.S. At the end of six months she was much improved: monthly examinations showed the C.S.F. to be normal.

Case 29.—A female infant aged 9 months. In the second week of treatment she had a convulsion with a residual spastic paresis of the left arm and leg. On the 644th day of observation she was much improved and could walk and run; only slight spasticity of the left arm remained. She was partially deaf and slightly retarded mentally, and was given one "cytacon" tablet daily (10 mg. of vitamin B_{12}), with beneficial effect: she is now much more active and alert, and is attempting to talk.

Table II shows the details of the 35 cases.

Discussion

During streptomycin–P.A.S. treatment rashes, fever, loss of weight, anorexia, vomiting, vertigo, deafness, and albuminuria occur in varying degrees. With the exception of deafness most of these symptoms subside when the streptomycin is stopped. The rashes usually respond to antihistamine drugs; these substances have also been used by various authorities for the treatment of vertigo and deafness, but definite conclusions have not yet been reached.

Marked degrees of hearing loss and partial deafness form the one serious complication which occurs in cases otherwise fit and well. Although the evidence is at present conflicting, it would certainly seem that the auditory nerve as well as the vestibular nerve is affected in some cases, and the general consensus is that the neurotoxic streptomycin may be responsible. Whilst it is impossible to say that the severe degree of deafness will be permanent, the rate of recovery is extremely slow and the education of the affected children would certainly suffer without special educational treatment. This is particularly so with very young

TABLE II.—*Details of the 35 Cases*

Case No.	Age (Years)	Sex	History (Days)	Condition on Admission	Mantoux Test	Chest X-ray	History of Contact	Direct Exam. of C.S.F. for T.B.	Culture of C.S.F. for T.B.	Streptomycin Treatment (Days)	Days of Observation	Result
1	2	M	14	A	1/10,000+	Miliary	0	0	+	166	756	Full recovery
2	28	M	14	A	1/1,000+	Phthisis	0	+	+	141	300	Full recovery. C.S.F. normal. Sputum negative
3	11	M	21	A	1/1,000+	P.C.	0	+	+	120	121	Died
4	14	M	28	A	1/1,000+	Too ill	+	+	+	17	17	,,
5	2	M	28	A	1/1,000+	,, ,,	+	+	+	19	19	,,
6	1 10/12	F	24	M	1/1,000+	Miliary	0	0	0	23	23	Died. P.M. showed tuberculous meningitis
7	2	F	12	A	1/1,000+	,,	+	+	+	18	21	Died
8	6	M	12	M	1/1,000+	P.C.	+	+	+	160	420	Relapsed and died 9 months after completion of treatment. P.M. showed tuberculoma of brain
9	48	M	14	A	1/1,000+	Phthisis	0	+	+	6	6	Died
10	20	F	5	A	1/1,000+	0	0	+	+	179	581	Recovery. Right hemiplegia, much improved on 580th day. C.S.F. normal
11	2 4/12	F	11	A	1/1,000+	P.C.	0	0	+	168	910	C.S.F. normal. Full recovery
12	16	M	20	M	1/1,000+	0	0	+	+	162	626	,, ,, ,,
13	3	M	21	A	1/1,000+	Miliary	0	0	+	161	850	Recovery. Tuberculous ankle healed
14	11 9/12	F	13	A	1/100+	,,	0	+	+	126	667	C.S.F. normal. Full recovery
15	1	M	10	M	1/1,000+	P.C.	+	0	+	167	584	Recovery. Mentally retarded. Difficulty in walking. Improving. C.S.F. normal
16	15 6/12	M	6	A	1/1,000+	,,	0	+	+	155	517	Recovery. Partial deafness but improving. C.S.F. normal
17	13	F	7	M	1/1,000+	0	0	+	+	160	437	C.S.F. normal. Full recovery
18	2	M	10	A	1/1,000+	P.C.	0	0	+	160	812	,, ,, ,, ,,
19	19 6/12	F	10	M	1/1,000+	0	0	0	+	160	599	,, ,, ,, ,,
20	7	M	7	M	1/10,000+	0	+	0	+	157	868	,, ,, ,, ,,
21	22	M	14	M	1/10,000+	P.C.	+	0	+	162	370	,, ,, ,, ,,
22	17	F	14	A	1/1,000+	0	0	+	+	168	370	,, ,, ,, ,,
23	5 11/12	F	11	A	1/1,000+	0	+	+	+	168	390	,, ,, ,, ,,
24	23	F	7	A	1/10,000+	0	+	+	+	168	370	,, ,, ,, ,,
25	1 11/12	M	14	A	1/1,000+	P.C.	0	+	+	168	639	Recovery; mentally retarded. C.S.F. normal
26	6	F	5	E	1/10,000+	,,	+	0	0	170	370	Full recovery. C.S.F. normal
27	18	F	14	A	1/1,000+	,,	+	+	+	170	370	Recovery; partial deafness. C.S.F. normal
28	14	F	14	M	1/1,000+	Miliary	0	0	0	160	740	Readmitted 6 months after discharge with miliary tuberculosis of lungs. Much improved with 2nd course dihydrostreptomycin. C.S.F. normal
29	9/12	F	7	M	1/10,000+	P.C.	+	0	+	160	644	Recovery. Left hemiplegia. Much improved. C.S.F. normal
30	2 6/12	M	14	M	1/10,000+	,,	0	0	+	160	370	C.S.F. normal. Full recovery
31	2 6/12	M	6	A	1/1,000+	0	0	0	0	168	370	,, ,, ,, ,,
32	3	M	8	E	1/10,000+	P.C.	+	+	+	164	370	,, ,, ,, ,,
33	14	M	12	M	1/10,000+	0	0	0	0	164	370	,, ,, ,, ,,
34	8	M	7	M	1/1,000+	P.C.	+	0	+	168	387	,, ,, ,, ,,
35	10	M	14	A	1/1,000+	Miliary	0	+	+	168	370	Recovery. Partial deafness. C.S.F. normal

E=Early case. M=Middle case. A=Advanced case. P.C.=Primary complex. Miliary=Miliary disease of lungs.

children whose early appreciation of speech has been insufficient to give them any permanent memory of sound.

Some authorities believe that the deafness is due to the tuberculous process and support this by the fact that streptomycin has been extensively used for other forms of tuberculous disease and, whilst admitting damage to the balancing mechanism in the inner ear, affirm that it is not a cause of deafness when used in the normal dosage.

The occurrence of deafness in cases of tuberculous meningitis treated with streptomycin shows considerable variation in incidence from place to place, and in order to obtain reliable statistics it would be necessary to do objective tests of hearing in all cases, otherwise cases of high-frequency deafness might easily be missed.

As regards the mental impairment following tuberculous meningitis, it is difficult to assess in some cases owing to motor disability and poor hand–eye co-ordination. Objective assessment as compared with pre-illness history would indicate some impairment of intellectual functioning in certain cases, but repeated follow-up examinations are necessary to ascertain whether this is likely to be permanent.

The marked increase in weight in marasmic babies after intramuscular injections of vitamin B_{12} was noted and it was decided to give all cases of tuberculous meningitis showing muscular wasting one tablet of cytacon daily. In addition to increased weight gain (Table III) patients also showed increased activity and alertness and definite increase in appetite.

TABLE III.—*Weight Record Following Oral Vitamin B_{12}*

Case No.	Before Treatment	1st Week	2nd Week	3rd Week	4th Week	5th Week	6th Week	7th Week	8th Week
	st. lb.	st. lb.	st. lb.	st. lb.	st. lb.	st. lb.	st. lb.	st. lb.	st. lb.
26	3 7	3 8	3 7	3 8	3 8	3 9	3 9	3 9	3 9
27	7 5½	7 7	7 7	7 8	7 9	7 11	7 11	7 11	7 12
29	2 0	2 1½	2 2	2 2	2 1	2 2	2 2	2 1	2 2
30	2 5	2 5	2 6	2 7	2 6	2 6	2 7	2 7	2 7
31	1 12	1 12½	1 13	1 12	1 12	2 1	2 1	2 2	2 3
32	2 8	2 8½	2 8	2 8	2 8	2 8	2 8	2 8	2 8
33	7 9	7 10½	7 10	7 11	8 1	8 5	8 6	8 6	8 9
35	5 6½	5 6½	5 7	5 7	5 7	5 8	5 10	5 10	5 10

Various writers on the treatment of tuberculous meningitis have stressed the disturbing and severe strain on the nursing staff attending these cases, but in this hospital the daily lumbar puncture for six months is accepted by patients and staff as a normal routine procedure. Apart from the actual lumbar puncture session, the tuberculous meningitis ward is one of the most cheerful wards in the hospital. This is all due to the extremely kind and efficient methods of the matron, Miss D. H. Dronfield, and her nursing staff, and their own inward satisfaction at seeing results impressive for a disease which until the last few years was usually fatal.

CHLORAMPHENICOL IN TREATMENT OF CUTANEOUS ANTHRAX

BY

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Chloramphenicol in concentrations of 5 μg./ml. has been shown to inhibit *in vitro* several strains of *Bacillus anthracis*, one strain being rather more susceptible (McLean, Schwab, Hillegas, Schlingman, 1949). Its clinical effect was therefore tried on four cases of cutaneous anthrax in Indian labourers.

Case 1

An Indian labourer was admitted to hospital on June 7, 1950, in a restless comatose condition. His temperature was 96° F. (35.6° C.), pulse 74, and respirations 30. The spleen was palpable. On examination the pulmonary condition was normal. A blood slide showed the presence of malaria parasites. Kernig's sign was positive and neck rigidity was present. There was a vesicular pustular eruption with an oedematous base over the proximal end of the left fibula. A smear from this sore showed *B. anthracis* ++. He was treated with "acetylarsan," 3 ml. intramuscularly, and procaine penicillin in oil, 300,000 units. Sustaining measures and lumbar punctures were impossible owing to his restlessness, and he died seven hours after admission. Post-mortem examination was refused. A provisional diagnosis of anthrax meningitis, with possibly intestinal anthrax, was made.

Immediate inquiries elicited that a cow had died under suspicious circumstances seven days previously, and that he, with about 50 others, had cut it up and eaten it. All these contacts were immediately examined, and four further cases of anthrax were discovered. All belonged to the scavenger class.

Case 2

A man aged 35 was admitted at 7 p.m. on June 7. There was a history of carving and eating the same cow. His temperature was 100° F. (37.8° C.), pulse 100, and respirations 28. He was anaemic, and his heart was slightly enlarged (a usual condition in these people). There was a sore on the left thumb ½ in. (1.25 cm.) in diameter which had been present for a week. It had started, after some itching, as a circular red papule; it had then become vesiculated and a dark scab had formed in the centre. By this time the base was very oedematous and the whole sore steadily grew bigger, the scab softening and becoming a dirty colour rather than black; a number of surrounding vesicles became confluent and exuded serum. The regional lymph nodes were not enlarged or tender. There was a second oval sore 2½ in. (6.3 cm.) long on his back, and a third on the lateral aspect of the left knee. Slides from all three sores showed a heavy infection of anthrax.

He was treated on traditional lines with procaine penicillin in oil, 300,000 units daily for seven days. Sulphadiazine was given as follows: 3 g. immediately, 1 g. four-hourly for three days, and 1 g. thrice daily on the fourth day. Acetylarsan, 3 ml., was given on the first day and neoarsphenamine, 0.3 g., on the second day. Neoarsphenamine, 0.15 g., was given on the fourth and eighth days. The temperature and pulse settled to normal by the fourth day, and all sores had diminished in size; oedema was much less. The cultures remained positive until the ninth day and were thereafter negative. All sores were healed on the twenty-fifth day.

Case 3

A girl aged 12 was admitted on June 7 with a sore over the insertion of the left deltoid. She had eaten some of the same cow, and her brother (Case 4) was also affected. The sore had started with an itching place, and a circular red papule soon appeared. On June 4 this had grown and become vesicular. On her admission there was a depressed black scab at the centre surrounded by a confluent unbroken vesicle ½ in. (1.25 cm.) in diameter, the whole lying on an oedematous base. One secondary papule was present immediately outside the ring of vesicles. Her temperature was 100° F. (37.8° C.), pulse 104, and respirations 39. The regional lymph nodes were enlarged and tender. A slide showed *B. anthracis* +.

Chloramphenicol, 1.75 g. (60 mg. per kg. of body weight) orally, divided into four doses given every hour, was administered that night, and 750 mg. (26 mg./kg.) thrice daily was started next day and continued for three days. The doses were then reduced to half this amount for a further three days. Pulse and temperature were normal by the fourth day, and the sore had dried up; oedema had disappeared and the slide was negative for anthrax. On the thirteenth day the lymph nodes had entirely subsided and the scab separated, and slide and culture were negative for *B. anthracis*. All sores were completely healed on the twenty-third day.

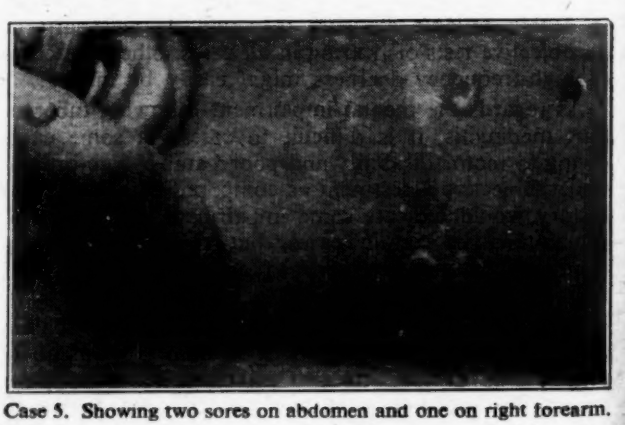
Case 4

A boy aged 10 was admitted on June 7 with a history identical to that of his sister (Case 3). On admission he had a sore measuring 1¼ by 1¼ in. (3.2 by 4.4 cm.) on the back of his knee. In the centre there was a dark tough scab which was surrounded by a vesicle that had burst. The base was grossly oedematous. The regional glands were enlarged and tender. His temperature was 100° F. (37.8° C.), pulse 108, and respirations 32. A slide showed *B. anthracis* +.

Chloramphenicol, 1.25 g. (52 mg./kg.) divided into four doses, was given at hourly intervals, and from next morning 620 mg. (26 mg./kg.) thrice daily was given for three days, and then the dose was halved for two days and finally reduced to 60 mg. thrice daily for three days. The temperature had settled by the second day, and on the third day the slide was negative. By the fourth day there was much less oedema, and the sore was cleaner. On the eighth day a culture gave a positive result, but thereafter eight daily cultures were negative. He made an uneventful recovery, and all sores were completely healed on the twenty-ninth day.

Case 5

An infant aged 10 months was admitted on June 7. There was no history of eating or handling affected meat. Case 2 stated that after he had cut off his portion from the cow and taken it home he had taken the infant on his knee and played with it. The mother, who had cooked and eaten the meat and had nursed the child at the breast throughout the whole illness, was not affected. Four sores were present—two on the abdomen each 1 in. (2.5 cm.) in diameter, one on the right forearm ½ in. (1.25 cm.) in diameter (see illustration), and a small sore starting on the



Case 5. Showing two sores on abdomen and one on right forearm.

leg. The temperature was 100° F. (37.8° C.), pulse 150, and respirations 50. A slide showed *B. anthracis* +.

Chloramphenicol, 0.375 g. (64 mg./kg.), was given in powder form followed immediately by breast-feeding. No further dose was given that night. From next morning 188 mg. (32 mg./kg.) thrice daily was given for 60 hours; then the dose was reduced by half for a further 60 hours and again halved for a further 48 hours. On the second day the temperature was 102° F. (38.9° C.), pulse 160, and respirations 50. The sores and the general condition were the same. A slide showed *B. anthracis* ++. Next day the general condition was the same except for mild diarrhoea. The sore on the leg had not increased in size, but a vesicle had formed and burst. A slide showed *B. anthracis* +. On the fourth day the general condition was good, the diarrhoea less, all sores were slightly smaller, and the leg sore was drier. The dark scabs were more pronounced. On the fifth day the general condition was good, stools were normal, and the sores dry. A negative slide but positive culture were found on the eighth day by lifting the scab and culturing the underlying pus. Thereafter the sores gradually healed. All further slides were negative, but a further positive culture was obtained on the thirteenth day. Cultures on the ninth, tenth, fourteenth, and fifteenth days were negative. A peculiarity of this case was the persistently oedematous base, which only gradually subsided, whereas in the other cases oedema disappeared rapidly. After some secondary infection the sores were completely healed on the thirty-ninth day.

Case 6

A man aged 55 was admitted to hospital on July 8 with a sore on his back and with fever. This was an isolated case occurring in a different district in a member of a different caste. On July 3 he had felt an itching on his back and rubbed it. He then noticed a lump and a vesicular sore on his back. This gradually enlarged, and on July 5 he felt feverish. There was no history of how the infection could have occurred. On admission a malignant pustule was seen on his back about 3 in. (7.5 cm.) above the right iliac crest, in the same position as one of the sores in Case 2, and presumably caused by carrying infected meat on the back. The sore measured 1¾ by 1½ in. (4.4 by 3.8 cm.) and had a black centre surrounded by ruptured vesicles exuding serum. The skin surrounding the sore was oedematous for about 12 in. (30 cm.) and for a rather greater distance downwards and over the abdominal wall. The right axillary glands were enlarged and tender. The spleen was not palpable. His temperature was 101.4° F. (38.6° C.), pulse 90, and respirations 28. His weight was 112 lb. (50.9 kg.). A slide was negative for *B. anthracis*, but culture was positive.

Treatment was not given on July 9 owing to administrative difficulties. On July 10 chloramphenicol, 3.25 g. (64 mg./kg.) divided into four doses was given every hour. Nothing further was given that night. On July 11, 12, and 13, 1.5 g. (29.6 mg./kg.) was given thrice daily. The dose was halved on July 14 and 15. On July 10 his temperature was 101.4° F. (38.6° C.), pulse 80, and respirations 20. The sore looked slightly bigger and had an angry-looking edge with increased serous discharge. The pain and irritation were more marked. The oedema had spread round to the nipple and was more pronounced. Regional lymphadenitis was increased. A slide was negative for *B. anthracis*, but culture was positive. Next day, 12 hours after starting treatment, there was a dramatic improvement: the sore was the same size, but there was no pain or itching, the serous discharge was less, the central slough rather bigger, and oedema had definitely diminished in area and severity. Regional lymph nodes were smaller and not tender. On July 12 further rapid improvement occurred. A slide and culture were negative. All further slides and cultures were negative. On July 13 there was no oedema. The whole sore was dry and covered by a black scab.

The patient was discharged on July 19 to the out-patient department. On discharge he still had a slightly enlarged axillary gland and the sore was covered with a firmly adherent tough black scab measuring 1½ by 1 in. (3.8 by 2.5 cm.). The wound healed in the usual fashion.

Discussion

The opportunity given by a small outbreak of anthrax was used to test the clinical efficiency of chloramphenicol in cutaneous anthrax. Except for Case 1, in which the patient was *in extremis* on admission and died, all cases recovered. Only Case 1 had an enlarged spleen, and the disease appeared to be limited to the skin; but, owing to a lack of blood culture facilities, septicaemia cannot be entirely excluded. The small proportion of those affected compared with those at risk and the continued exposure of the mother of Case 4 raise a suspicion that these Indian labourers have a certain amount of resistance against acquiring this infection. Experience at other times has shown that the untreated disease is uniformly fatal. Case 1 shows that the strain was a virulent one.

Clinical appearances were typical of anthrax. All smears showed the typical morphological characters, and cultures on nutrient gelatin gave the typical spore-forming organism. Capsules were demonstrated by polychrome staining, and the suspensions of the cultures were positive to the malachite green test.

Summary

Cutaneous anthrax in four patients aged from 10 months to 55 years was treated with chloramphenicol with an initial dose of 60 mg. per kg. of body weight and a maintenance dose of 30 mg./kg. eight-hourly for 60 hours, then 15 mg./kg. eight-hourly for 48 hours, and finally 7.5 mg./kg. eight-hourly for a further 48 hours. All four cases showed rapid improvement leading to cure.

One case was treated on the usual lines with penicillin, sulphadiazine, and arsenic as a control. The series is too small to demonstrate the superiority of either method, each appearing equally effective.

It is a pleasure to acknowledge the help given by Messrs. Parke, Davis and Co., who supplied the chloramphenicol ("chloromycetin") and obtained permission from the Government of India to use it in these cases.

REFERENCE

McLean, I. W., jun., Schwab, J. L., Hillegas, A. B., Schlingman, A. S. (1949). *J. clin. Invest.*, **28**, 953.

The medical section of the Library Association will hold its first week-end conference at University Hall, Liverpool, from Friday evening, March 28, to Monday midday, March 31. The programme will include an address by Sir Henry Cohen on the romance of words; a symposium on three types of medical libraries by Miss I. B. Jones, Mr. W. A. Lee, and Mr. G. Wilson; visits to the libraries of the Liverpool Medical Institution, Liverpool University, and the School of Tropical Medicine, and to the Speke Works of Evans' Medical Supplies. There will be a reception at the Liverpool Medical Institution, a visit to Speke Hall, and a coach excursion to Llangollen. Attendance at the conference is open to medical men as well as to librarians, and those who are interested are invited to write to the hon. secretary of the Medical Section of the Library Association, c/o the British Dental Association Library, 13, Hill Street, London, W.1.

BLEEDING MECKEL'S DIVERTICULUM

A REPORT OF TWO CASES

BY

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A Meckel's diverticulum remains as a vestigial remnant of the vitelline duct in between 1 and 2% of individuals; Harkins (1933) found the anomaly in some form in 1.3% of over 25,000 necropsies.

Intestinal obstruction is said to be the most common complication (Taylor, 1947; Haber, 1947), but out of 1,605 cases from the literature Moses (1947) found that the presenting disorder was haemorrhage in 496 (30.9%), intestinal obstruction in 383 (23.8%), perforation in 222 (13.8%), a Littré's hernia in 188 (11.7%), and diverticulitis in 165 (10.3%). The incidence of the whole group of disorders is more than twice as great in males as in females.

In the cases here reported the bleeding was intractable and required urgent surgical intervention.

Case 1

A salesman aged 27 was admitted to the Royal Victoria Infirmary under Dr. A. G. Ogilvie on the morning of August 23, 1950. He had woken feeling nauseated, weak, and faint, and perspiring profusely. On going to the w.c. he passed a large amount of dark semi-fluid material per rectum.

Five years previously, while in the Army in India, he had had a similar experience and had received a blood transfusion. Investigation revealed no gastro-intestinal abnormality. For the past two years he had had vague lower abdominal discomfort after meals.

On examination he looked healthy, not evidently in pain. The pulse rate was 64 a minute, blood pressure 120/70. Abdominal palpation revealed nothing significant, but on rectal examination the examining finger was stained with dark-red blood. No other physical abnormality was noted.

The haemoglobin on admission was 75% (11.25 g./100 ml.), Hess's capillary fragility test was negative, and the bleeding and clotting times were normal.

Some four hours after admission the patient suddenly became pale, anxious, and sweating; the pulse rate rose to 96, and the blood pressure fell to 100/50. Ten minutes later he passed much dark-red blood per rectum. After a transfusion of 2 pints (1.14 litres) of compatible whole blood he improved. It was thought that the bleeding was from a duodenal ulcer, an intestinal polyp, or a Meckel's diverticulum.

The following day he again had a severe haemorrhage, necessitating further transfusion. Professor F. H. Bentley was consulted, and agreed that if there was evidence of further bleeding an emergency laparotomy should be performed. Radiographic examination, gastroscopy, and sigmoidoscopy were, for obvious reasons, not carried out.

On the morning of August 27 the patient again had a severe haemorrhage; his haemoglobin fell to 56% (8.4 g./100 ml.), and another continuous drip transfusion was begun.

Operation.—At 3 p.m. Professor Bentley opened the abdomen through a right para-umbilical paramedian incision; the posterior wall of the duodenum was felt to be a little thickened, but no ulcer appeared to be present. The caecum and lower ileum were filled with blood. Some 2 ft. (61 cm.) above the ileo-caecal valve a Meckel's diverticulum, about 4 in. (10 cm.) in length, was found protruding from the antimesenteric border of the gut. Blood filled the diverticulum and the ileum for some 12 in. (30.5 cm.) proximal to it; above this point the bowel was collapsed. Since it was evident that the diverticulum was the site of the haemorrhage it was excised.

The mucosa of the last inch (2.5 cm.) of the diverticulum showed multiple petechial haemorrhages and two superficial ulcers each about 3 mm. in diameter; in the base of one of these could be seen the mouth of a small vessel. The proximal portion was macroscopically normal. Dr. A. H. Cameron reported that histological examination showed acute ulceration, with no evidence of gastric heterotopia.

The patient made a good recovery, although gastric aspiration and intravenous therapy were necessary for 36 hours owing to moderate abdominal distension. The stools were free from occult blood within five days. On discharge on September 11 he felt well and his haemoglobin was 96% (14.4 g./100 ml.).

Case 2

A male telephonist aged 17 was admitted to the Royal Victoria Infirmary at 2.30 a.m. on July 15, 1951, under the care of Mr. John Brumwell. He had been perfectly well until two days before admission, when he began to pass small quantities of dark-red blood per rectum. This was unaccompanied by other symptoms until 24 hours later, when he began to feel weak and faint and to sweat profusely. At 1.45 o'clock on the morning of admission he woke with an urgent desire to move his bowels, fainted on getting out of bed, and passed a further large quantity of dark-red blood.

On admission he was anxious, sighing, and restless but not in pain. His conjunctivae and mucous membranes were blanched, pulse rate 120, and blood pressure 100/60. There was no tenderness or mass on abdominal palpation, but on rectal examination the examining finger was stained with dark-red blood.

A blood transfusion was begun immediately, and over the next 24 hours he received 9 pints (5.1 litres) of whole blood, with considerable improvement. At one stage his haemoglobin had fallen to 45% (6.5 g./100 ml.).

On July 20 he was transferred to a medical ward for investigation under the care of Dr. A. G. Ogilvie. His general condition was then good; pulse 85, blood pressure 130/70, and haemoglobin 66% (9.5 g./100 ml.).

Two days later he suddenly became weak and faint, vomited clear watery material, and passed a large dark-red fluid stool; despite continuous transfusion the bleeding continued. The clinical picture was so reminiscent of Case 1 that a firm clinical diagnosis of bleeding from a Meckel's diverticulum was made. Mr. Denis Hindmarsh was consulted, and agreed to carry out laparotomy.

Operation.—The abdomen was opened through a right paramedian incision. The large intestine and lower ileum were found to be filled with blood. A Meckel's diverticulum was identified, about 2 in. (5 cm.) in length, and the distal end was clearly thickened; it was removed together with a "wedge" of intestinal wall.

Dr. J. Hart Mercer reported on the specimen as follows: "The diverticulum shows a fairly deep oval ulcer in the floor of which no obvious vessel is visible to the naked eye. The mucosa macroscopically is mostly of the small intestinal type, but at the edge of the specimen some distance from the ulcer a thicker mucosa of more luxuriant appearance is seen. Histological examination reveals an active chronic peptic ulcer: the mucosa immediately surrounding it is of intestinal type, but further away gastric mucosa is seen."

The patient made a good and uneventful recovery from the operation, and on discharge on August 3 his haemoglobin was 89% (12.9 g./100 ml.).

Discussion

In the reported cases of haemorrhage from a Meckel's diverticulum a correct pre-operative diagnosis has rarely been made, except in children. In Case 1, although ulceration in a diverticulum was considered as a possibility, no firm diagnosis was reached before operation; in the second case, however, the similarity of the clinical picture to that in the first patient was striking and enabled the diagnosis to be made confidently. The character of the blood passed per rectum weighed heavily in pointing out the offending organ; it was dark red in colour, intermediate between the characteristic tarry stool of melaena from a duodenal ulcer and the bright-red blood of haemorrhage from a lesion of the colon. This point has been stressed by Murray (1947). A second feature of value in the differential diagnosis was that both patients vomited clear watery fluid containing no blood.

Schaetz (1925) described the presence of areas of heterotopic gastric mucosa in 5 out of 30 diverticula examined, and it has been assumed that, as occurred in our Case 2, haemorrhage is invariably the result of ulceration in or around such islands (Haber, 1947; Taylor, 1947). However, Chesterman (1935) pointed out that ulceration can occur in the absence of gastric mucosa, explained by Winkelbauer (1929) as being due to irregular peristalsis producing invagination of the apex of the diverticulum; this is possibly the explanation in Case 1, as the lesions were confined to the tip.

Haemorrhage from a Meckel's diverticulum may produce a serious threat to life. It should be suspected in patients suffering from melaena of the type described; if haemorrhage is recurrent laparotomy is indicated, since the risks of an adequately performed operation are slight. If surgical treatment is not required in the acute stage a Meckel's diverticulum may occasionally be demonstrated radiologically (Rousseau and Martin, 1943).

Summary

Two cases of bleeding due to ulceration in a Meckel's diverticulum are reported. Cure followed excision of the diverticulum in each case.

One specimen showed acute ulceration and no gastric heterotopia; the other contained gastric mucosa, and a chronic peptic ulcer was present.

It is suggested that the character and colour of the blood passed per rectum—that is, dark red, as distinct from the tarry stool of a duodenal ulcer and the bright-red blood of a colonic lesion—may enable this syndrome to be diagnosed pre-operatively.

We are indebted to Dr. A. G. Ogilvie for permission to publish these cases, to Professor F. H. Bentley and Mr. Denis Hindmarsh for details of the surgical treatment, and to Dr. A. H. Cameron and Dr. J. Hart Mercer for the pathological reports.

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Medical Memoranda

Accelerated Ossification in a Cretin caused by High Thyroid Dosage

The following case is reported because it is not generally known, and is not cited in paediatric textbooks, that high thyroid dosage in cretinism may cause advanced ossification, and because it demonstrates the advisability, during treatment, of taking serial radiographs of the ossific centres if maximal dosage within the limits of clinical tolerance is to be given.

Case Report

The patient was a full-term female infant with a birth weight of 6 lb. 13 oz. (3.1 kg.). She came under observation at 14 weeks of age, when the mother reported that the baby had seemed normal until 10 to 12 weeks, when she became drowsy, stopped smiling, lost interest, developed a feeble hoarse cry, and altered in facial appearance. These symptoms had since progressed, and on examination the baby, which then weighed 8 lb. 7 oz. (3.8 kg.), was seen to be a typical cretin (Figs. 1 and 2), with lethargy, coarse expressionless features, thick protruding tongue, dry yellow skin, puffy hands, large abdomen, and umbilical hernia. She did not watch other persons, the eyes did not follow a moving object, and there was no smile. In the prone position the head slumped down, and in no position of the body was it held steady. Radiographs showed gross delay in ossification in that no centres were visible for the cuboids, the heads of the tibiae, or the wrists.

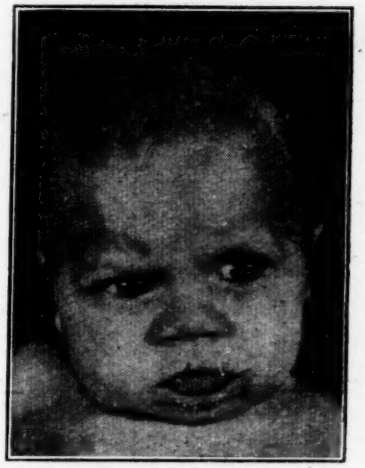

FIG. 1.—Face of the child at 14 weeks.

It was decided to increase thyroid dosage as quickly as practicable to the limits of clinical tolerance on the grounds (*a*) that often the mental development of cretins does not progress favourably on the customary schedules even when treatment begins early (Warkany, 1950); (*b*) that some poor results may be due to underdosage attributable to faulty assay, deterioration, or impaired absorption; and (*c*) that other poor results may be due to initial slowness in building the dose to a maintenance level.

The initial treatment took place in hospital, dry thyroid (*B.P.*) being given in doses of 1/10, ⅛, ¼, and ½ gr.

FIG. 2.—The child at 14 weeks.

(6.5, 8, 16, and 32 mg.) on the first, second, third, and fourth days, respectively, and then ¼ gr. (32 mg.) on each of the remaining 14 days of the in-patient period: the subsequent increments (see Table) were prescribed from the out-patient clinic. Within 19 days of the beginning of

Dosage of Dry Thyroid and Weight of Infant

Age in Months	Average Daily Dose of Dry Thyroid (*B.P.*)	Weight
5–6	1·2 gr. (78 mg.)	At 6 months 12·1 lb. (5·49 kg.)
7–8	1·7 „ (110·5 mg.)	„ 8 „ 14·6 „ (6.62 kg.)
9–10	2·2 „ (143 mg.)	„ 10 „ 18·8 „ (8.53 kg.)
11–12	2·8 „ (182 mg.)	„ 12 „ 22·2 „ (10·07 kg.)

treatment the typical therapeutic response was obvious and the baby improved dramatically in appearance and general symptoms. She continued under close observation, being examined and weighed at weekly intervals, and the parents, who were regarded as reliable observers, were informed of the issues and asked to report any looseness of the motions, undue sweating, restlessness, or other untoward symptom which could be regarded as evidence of intolerance to the increasing thyroid dosage. They also recorded the sleeping pulse rate.

No clinical evidence of intolerance did, however, occur, even though an average daily dose of 2.8 gr. (182 mg.) was reached during the eleventh and twelfth months; it was at this stage decided to make no further increase. At 15 months radiographs of the wrist (Fig. 3) showed that ossification, which had initially been retarded, was now very advanced. Six carpal centres were present as well as those for the lower end of the radius and the head of the fifth metacarpal. According to the standards described by Todd (1937), ossification had therefore advanced to a degree expected in a female child of 4 years 3 months. The patient's length, which was 22¼ in. (57.2 cm.) at 18 weeks of age, was now 31 in. (78.7 cm.) and her weight was 23½ lb. (10.7 kg.).

FIG. 3.—Radiograph of wrist at 15 months.

From 15 months of age the thyroid dose was substantially reduced, but her bone age at 3 years was still advanced, being equivalent to that of a child of 5 years 9 months (Todd, 1937). Her height was 39¼ in. (99 cm.). A satisfactory aspect of the case was that the child's mental development seemed to be within normal limits and she was also tall, but a future possibility which must be considered is that of premature union of the epiphyses with the diaphyses of the growing bones.

ADDENDUM.—Since the submission of this report for publication attention has also been drawn by Drs. B. Schlesinger and O. D. Fisher (*Lancet*, 1951, 2, 289) to the acceleration of ossification that may follow high thyroid dosage in cretinism.

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Bacterial Endocarditis Caused by Coagulase-Negative Staph. Albus

Matthew (1951) reports two fatal cases of bacterial endocarditis in which the infecting organism was a coagulase-negative *Staphylococcus albus* and comments on the rarity of this organism as a cause. A similar case is here presented with brief clinical details; recovery took place after treatment with penicillin and streptomycin.

Case Report

A man aged 72 was admitted to hospital on August 18, 1950. He gave no past history of acute rheumatism, but had had an attack of mild congestive failure after unwonted exertion two years before; at this time an apical systolic murmur was heard and an *x*-ray film showed cardiac enlargement; recovery was rapid and no further symptoms occurred.

The present illness started four weeks before admission, with fever up to 101° F. (38.3° C.), general malaise, headache, night sweats, and shooting pains in the hands and legs; the serum twice showed no agglutination with enteric, salmonella, or brucella organisms. The patient gave no history of furunculosis, but his wife had a whitlow during the month preceding his illness.

On examination general appearances were normal except for some pallor of mucous membranes. His temperature was 99.4° F. (37.4° C.), pulse rate 100, and respirations 22. Clinical enlargement of the heart was noted, a systolic murmur was heard over most of the praecordium, and a soft diastolic murmur, which became much louder in the course of a week, down the left side of the sternum. The spleen was just palpable. No finger-clubbing or peripheral embolic phenomena were found, though a week after admission a small subconjunctival petechial haemorrhage was noted. His blood pressure was 150/80; E.S.R. (corrected), 18 mm. in one hour; R.B.C., 4,400,000; Hb, 74%; W.B.C., 9,400 (neutrophils 85%); and urine deposit showed occasional red cells. Blood culture gave a haemolytic coagulase-negative *Staph. albus*; this was repeated with a similar result. The organism was insensitive to "sulphatriad," moderately sensitive to "aureomycin," chloramphenicol, and streptomycin, and sensitive to 6 units of penicillin in 1 ml. but insensitive to 3 units in 1 ml.

On August 23 penicillin, 1,000,000 units, soon increased to 2,000,000 and then to 4,000,000 units daily, was started. Three days later the patient complained of pain of indefinite type in his chest, but this quickly subsided and no evidence of pericarditis was found at any time. On September 3, as the temperature was still rising on most evenings to 100° F. (37.8° C.) or higher, streptomycin, 2 g. daily, was given in addition. Blood culture a week later was sterile, the spleen was no longer palpable, and the temperature gradually became and remained normal. A further blood culture was sterile, no R.B.C. were found in the urine, and Hb was 90%. Penicillin was discontinued on September 22 and streptomycin on October 13, and the patient returned home for further rest and convalescence.

It was soon necessary to readmit him for 14 days on account of acute dermatitis, which was thought to be possibly due to streptomycin and which responded to antihistamine drugs and local treatment. On returning home a second time he unluckily developed a small pulmonary embolus, but soon recovered. At the time of writing he is free of symptoms and leading a relatively active life.

I wish to thank Dr. Goodman Platts and Dr. Olive Cameron for pathological work and Dr. E. S. Vergette for clinical notes.

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Reviews

TO LOVE AND TO CHERISH

Patterns of Marriage. A Study of Marriage Relationships in the Urban Working Classes. By Eliot Slater, M.A., M.D., F.R.C.P., and Moya Woodside. (Pp. 311. 17s. 6d.) London: Cassell and Co. 1951.

This book tells how in 1943 Dr. Slater and Mrs. Woodside began collecting information about marriage. They took a sample of 100 neurotic soldiers and 100 physically ill soldiers (whether because of infection or injury at the front or from quiet areas) and interviewed them and their wives, seeking a full history and inquiring particularly into their marriage relationships. No unwilling informants were included. Most of the persons were from the manual-worker class, only 12 had matriculated, and fewer than 50 had been educated after the age of 14.

This must be one of the first works about marriage in this level of society. Its revelation of the drabness of pre-war working-class life and monotony at home, or toleration of disorder and despair, makes it a social document of importance. Astonishing numbers of people drift into acquaintanceship and after two years marry. But they seem to get married *for* something—a home—rather than *to* someone—their partner. One-fifth had married before the age of 21, three-quarters before 26. But, with marriage, culture ceased; women became tied to their homes in a way many are likely to refuse in future; religion interested few; politics reflected more often an emotional attitude to life than a considered outlook.

It is impossible to summarize the mass of statistically verified information we are given. For psychiatrists the book must be a tonic. Many opinions gained in the out-patient department or consulting-room are exploded. In theory, extramarital attachments were condemned by the subjects; practice proved somewhat different though not as different as might have been guessed. Less than 1 in 10 of the women had contracted forced marriages, a view suggesting some difference from that of the Registrar-General's report for 1937–8. Not 1 out of 100 neurotic men admitted impotence, but 1 out of 200 husbands admitted being henpecked. Past operations, especially gynaecological ones, impair orgasm in women. Mrs. Grundy is still rampant. Neither family doctors, health visitors, nor gynaecologists take adequate initiative to explain contraceptive techniques. Some of the happiest marriages were childless; no correlation was found between happiness and fertility. The authors are not pessimistic about the future. Despite overcrowding, conditions are improving, and higher standards of teaching may be expected to alter matters gradually. Further, despite tragic marriages, there are many surprising cases showing how difficulties have been surmounted or the expected separation did not occur.

It would be well to remember that the authors do not claim that their sampling was perfect. Factors such as prolonged absence from home, wartime work for women, and the roseate hues in which the dreary past were recalled make some of the information less reliable than the authors, or we, should like. But all social agencies will be grateful for this stimulating information, which we suspect Dr. Slater and Mrs. Woodside themselves hope will be questioned, criticized, and reflected upon to the encouragement of progressive social planning.

HENRY WILSON.

ARTIFICIAL IMMUNIZATION

Bacterial and Virus Diseases. Antisera, Toxoids, Vaccines, and Tuberculins in Prophylaxis and Treatment. By H. J. Parish, M.D., F.R.C.P.Ed., D.P.H. 2nd ed. (Pp. 204; illustrated. 10s. 6d.) Edinburgh: E. and S. Livingstone. 1951.

It is a mistake to suppose that chemotherapy has materially affected the usefulness of artificial immunization. The sulphonamides and antibiotics are mercifully most effective in just those conditions—pyogenic coccal infections, cerebrospinal fever, gonorrhoea, and anthrax—in which for one reason or another serum or other such treatment was least certain in its effects. The pre-eminence of immunization, both active and passive, in the treatment of diphtheria and tetanus remains unimpaired. The prophylactic value of vaccines is not diminished: indeed, the past few years have seen considerable advances in their application to whooping-cough, tuberculosis, and virus diseases. For those intending to make the best possible use of all such procedures in prevention and treatment and in the diagnosis of the immune state of the individual this book is an admirable guide. Although presenting theory adequately and clearly, it is essentially practical, since the author gives full instructions for carrying out every kind of injection or inoculation, defines the indications for them, and discusses such risks as may be involved and the precautions to be taken against them. He shows a nice discrimination in ignoring certain vaccines for whose use there is no favourable evidence, and in crediting to chemotherapy the major share in treating some of the infections for which antibacterial sera are also available.

L. P. GARROD.

THE CHORDATES

The Chordates. By Herbert W. Rand, Ph.D. (Pp. 862; 609 illustrations. £2 5s.) London: H. K. Lewis. 1950.

Not least of the features which raise Professor Rand's work above the general run of textbooks of vertebrate comparative anatomy is the fact that he can write really well. He recalls in his preface the days when students were few and had ample time to read, and, less nostalgically, the later expansion of university biology in America. "An earlier sense of freedom and leisure to work thoughtfully was insidiously superseded by a sense of crowding, pressure, and haste. . . . It was evident that the student of the later years was not reading much and could not be expected to." So he wrote the present book, to combine with an adequate factual content some discussion of the wider human significance of the subject.

In the first part he discusses the basic structure of vertebrates, in the second part the history and principles of comparative anatomy, and in the third the chordates, group by group. All of his well-chosen material is concisely, lucidly, and interestingly presented, and the text is accompanied by a wealth of good illustrations, including a photograph, which his students will treasure, of the author embroiled with a couple of chimpanzees.

Finally, in an epilogue entitled "What Comes of Studying Vertebrates," Professor Rand lets himself go. "The present classification of man as a primate mammalian chordate is based entirely on his bodily structure.

The ideal of modern classification is that it should express genetic relationship and that it should be so devised as to indicate the points where major and crucial evolutionary steps have been taken—i.e., the initiation of important new lines of specialization. The primates took such a step. Their shaping of the environment to their own uses is perhaps the most radical step in the whole course of evolution. . . . The time will come, and perhaps now is, when men should be assigned to an additional Class of vertebrates." And so he anticipates the erection of a new Class VII, Anthropoidea. The lemurs and tarsiers would remain among the mammals as an Order closely allied to the insectivores. The remaining primates would constitute the new Class, which would necessarily be subdivided into two subclasses. The first, including the monkeys and great apes, "could be called PROTOANTHROPOIDEA—a group analogous to SUBCLASS PROTOTHERIA of Mammalia." The second is to contain the present family Hominidae. "In some far-distant future, when man's social wisdom shall have so far caught up with his inventive intelligence as to justify the name for him, this SUBCLASS might be designated as SAPIENTIA."

G. P. WELLS.

BLOOD COAGULATION

Die Blutgerinnung in Theorie und Praxis. By Dr. Josef Schmid. Wiener Beiträge zur Inneren Medizin, Volume 4. (Pp. 444; 135 figures. M. 50.) Vienna: Verlag Wilhelm Maudrich. 1951.

The coagulation of the blood has become a matter of bewildering complexity. The simple equations formerly held to explain the process are now outmoded and new factors are constantly being discovered or, more precisely, their existence is constantly being inferred. If further evidence of this state of affairs were needed, it can be found in this book, in which the situation as it stood at the close of 1950 is adequately reviewed.

The author has forsaken the conventional arrangement of similar monographs, in which the physiology and biochemistry of the clotting process is first reviewed and is followed by a description of the clinical states which arise from its disturbance. After a brief historical review he devotes sections to the thrombokinases, prothrombokinase, and antithrombokinase, turning aside then to consider haemophilia, haemorrhagic states due to circulating anticoagulants, and thrombocytopenia. Then follow chapters on prothrombin, antiprothrombin, and vitamin K, succeeded by sections on hypothrombinaemia and the thromboses. He concludes with discussions of the prothrombin activators, fibrinogen, thrombin, thrombin inhibitor, clot retraction, and fibrinolysis.

The individual sections are full and up-to-date, but the arrangement is not entirely logical and robs the book of cohesion. There are detailed descriptions of technical methods which will be useful to the laboratory worker, but the clinician will need to seek enlightenment elsewhere. The book has the hallmarks of a painstaking compilation of other workers' observations and opinions, unleavened by critical selection. The reader who is not a professional "coagulationist" will regret the author's omission of a chapter in which the actual mechanism of clotting is described and the interrelationship of the many factors set out. His presentation conceals the unity of the process and tends to perpetuate the view that it consists of a number of asynchronous and almost unconnected reactions.

R. BODLEY SCOTT.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Diabetes Mellitus. By G. G. Duncan, M.D. (Pp. 289. 29s.) London: W. B. Saunders. 1951.

Transactions of the American Ophthalmological Society. 86th Annual Meeting, 1950. (Pp. 702. 97s. 6d.) London: Geoffrey Cumberlege. 1951.

Ocular Toxoplasmosis. By M. J. Hogan. (Pp. 86. 18s.) London: Geoffrey Cumberlege. 1951. (Available free of charge with the *Transactions of the American Ophthalmological Society* as above.)

Clinical Heart Disease. By S. A. Levine, M.D., F.A.C.P. 4th ed. (Pp. 556. 40s.) London: W. B. Saunders. 1951.

Principles and Practice of Obstetrics. By J. P. Greenhill, M.D. 10th ed. (Pp. 1,020. 60s.) London: W. B. Saunders. 1951.

The Glands Inside Us. By J. Ebling. (Pp. 94. 1s.) Thrift Books, No. 10. London: C. A. Watts. 1951.

Browsing Among Words of Science. By T. H. Savory, M.A., F.Z.S. (Pp. 94. 1s.) Thrift Books, No. 12. London: C. A. Watts. 1951.

The Juvenile Court, Today and Tomorrow. By J. Watson. (Pp. 40. 1s. 6d.) London: Clarke Hall Fellowship. 1951.

Directory and Handbook of the Scientific Instrument Manufacturers Association. (Pp. 251. Gratis.) London: Scientific Instrument Manufacturers Association. 1951.

New Biology. Edited by M. L. Johnson and M. Abercrombie. (Pp. 123. 2s.) Harmondsworth: Penguin Books. 1951.

Human Fertility: The Modern Dilemma. By R. C. Cook. (Pp. 351. 21s.) London: Victor Gollancz. 1951.

Low-Sodium Diet. By T. B. Rice, A.M., M.D. (Pp. 103. 19s. 6d.) London: Henry Kimpton. 1951.

The Medical Clinics of North America. Boston Number: Symposium on Specific Methods of Treatment. Edited by C. S. Keefer, M.D. (Pp. 347. No price.) London: W. B. Saunders. 1951.

Embryology of the Pig. By B. M. Patten. 3rd ed. (Pp. 352. 35s.) London: George Allen and Unwin. 1951.

Relief of Pain in Childbirth. By W. C. W. Nixon, M.D., F.R.C.S., F.R.C.O.G., and S. G. Ransom, M.R.C.S., L.R.C.P., D.A. (Pp. 109. 7s. 6d.) London: Cassell. 1951.

Ethylene and Propylene Glycols. By J. Rae, M.P.S. (Pp. 30. 2s. 6d.) London: The Pharmaceutical Press. 1951.

The Psychology of C. G. Jung. By Dr. J. Jacobi. (Pp. 204. 12s. 6d.) London: Routledge and Kegan Paul. 1951.

Genetic Neurology. Edited by P. Weiss. (Pp. 239. 37s. 6d.) London: Cambridge University Press. 1950.

Clinical Practice in Infectious Diseases. By E. H. R. Harries, M.D., F.R.C.P., and M. Mitman, M.D., F.R.C.P. 4th ed. (Pp. 717. 30s.) Edinburgh: E. and S. Livingstone. 1951.

Muir's Text-Book of Pathology. Revised by D. F. Cappell, M.D., F.R.F.P.S.G. 6th ed. (Pp. 1,090. 50s.) London: Edward Arnold. 1951.

Chest X-Ray Diagnosis. By M. Ritvo, M.D. (Pp. 558. 105s.) London: Henry Kimpton. 1951.

Proceedings of the First Conference on Electrokymography. Edited by B. R. Boone, M.D., and others. (Pp. 215. 75 cents.) Washington: U.S. Government Printing Office. 1951.

Technical Methods for the Technician. By A. L. Brown, B.A., M.D. 4th ed. (Pp. 784. $10.) Columbus, Ohio: A. L. Brown, Inc., 41, S. Grant Avenue. 1951.

Los Problemas Médicos en accidentes del Trabajo. By Dr. A. M. Barbero. (Pp. 236. No price.) Barcelona: Byp. 1951.

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VASCULAR SPASM

Knowledge of the peripheral circulation has been acquired slowly, and, despite a great volume of original work, facts of fundamental importance still elude discovery. From the time of William Harvey up to roughly the end of the nineteenth century the main interest of the circulatory physiologist was in the heart and great vessels. Only in the last thirty years or so has the work of Ebbecke, Krogh, Lewis, Gollwitzer-Meier, and a host of others directed attention to the more minute vessels. A variety of techniques have been used in the investigation of the circulation, and some of the more recently developed methods—notably the use of radiography of the larger vessels by Trueta and his associates[1] and, in the case of the minute vessels, the delicate micromanipulative techniques of Zweifach[2]—have given us a much more dynamic and detailed picture of the peripheral vascular tree. At the same time work with the radioactive isotopes has greatly expanded the scope of research, so that the complicated and continuously changing pattern of the circulation is now better understood.

At the risk of being dogmatic it may be said that, from the functional point of view, the peripheral circulation can be considered in three parts: first, the proximal vessels, changes in the calibre of which are chiefly passive in nature; secondly, the smaller arteries, veins, arterioles, and venules, which respond to both nervous and chemical stimuli; and, thirdly, the more minute vessels (capillaries, pre-capillaries, and metarterioles), which are subject to periodic changes in calibre, a phasic activity which has been termed "vasomotion." These last vessels, besides responding to the better-known nervous and chemical stimuli, are also influenced by enzymes such as renin, and the more recently described vasotropic factors V.E.M. (vaso-excitor material) and V.D.M. (vaso-depressor material). The clinician may find himself in danger of being overwhelmed by the many and varied additions to knowledge and sometimes be tempted to give too glib an explanation of certain manifestations of organic vascular disease. How often, for example, does he invoke "spasm" as an explanation of the otherwise inexplicable? Spasm has, in fact, become a medical *cliché*. Pickering[3] has recently referred to some common misconceptions about spasm in arterial disease and has emphasized how closely organic arterial occlusion can mimic vascular spasm. Similar misconceptions probably exist about the venous circulation, for Ochsner and de Bakey[4] have referred to the importance of spasm in venous thrombosis; yet it is very doubtful whether spasm plays any part in the majority of cases.

With so much interest in the minutiae of the circulation it is easy to assume that knowledge of the large vessels is fairly complete. That this is not so is shown in the opening pages of this issue by Mr. J. B. Kinmonth, who reports the results of some fundamental research into the behaviour of large arteries. It will be recalled that Trueta and his co-workers,[1] when investigating the crush syndrome, applied a tourniquet to the thighs of rabbits and observed, by a radiographic technique, contraction of the arteries in the contralateral limb—a finding which they attributed to reflex arterial spasm. The object of Mr. Kinmonth's investigation was to determine the cause and cure of spasm in the large arteries. By directly observing the femoral arteries in experimental animals whose blood pressure was recorded continuously, he has shown that the large arteries behave in a much more passive fashion than is commonly supposed. The changes in arterial calibre seen in Trueta's experiments are now known to be directly related to falling systemic blood pressure and not to reflex arterial spasm. It has further been demonstrated that neither faradic stimulation of the large arteries and lumbar sympathetic chain nor the intravenous injection of adrenaline has any direct effect on the diameter of the large arteries, although these stimuli can cause profound changes in the more peripheral vessels.

Many of these experimental findings in the rabbit have been confirmed in man, and Kinmonth has found that spasm of the proximal arteries can be induced only by direct trauma, the irritability of the vessels varying at different times and in different subjects. The upper part of the femoral artery has no vasoconstrictor nerves, and the exact level at which this nerve supply begins has not been determined. Wilde,[5] however, has shown by microdissection that the nerves to the upper femoral artery are purely sensory in character, and that vasoconstrictor fibres are distributed only to the more distal vessels and muscular tributaries. From the practical point of

1 *Studies of the Renal Circulation*, 1947, Oxford.
2 *Circulation*, 1950, **1**, 433.
3 *Lancet*, 1951, **2**, 845.
4 *J. Amer. med. Ass.*, 1940, **114**, 117.
5 *Brit. J. Surg.*, 1951, **39**, 97.

view this means that sympathetic nerve fibres are responsible for neither the initiation nor the maintenance of spasm in large arteries. This must necessarily influence treatment of the spasm which is sometimes seen in association with supracondylar fracture of the humerus and other types of direct arterial injury. Paravertebral block, peri-arterial stripping, and arteriectomy clearly have no place in treatment and are absolutely contraindicated. Early exploration and decompression of the affected artery is imperative, and Kinmonth has found that the local application of 2.5% papaverine sulphate solution is most effective in relaxing spasm. Locally applied procaine, caffeine, and warm saline packs are much less effective and less reliable, while the intravenous injection of papaverine sulphate is as ineffective in the human being as it is in the rabbit.

SHORTAGE OF X-RAY FILMS

The Ministry of Health stated recently: "There is a serious world shortage of *x*-ray films due to increasing usage in all countries. In this country usage during the first six months of 1951 was 16% greater than in the corresponding period of 1950 and was at a rate about 60% greater than in 1947."[1] Since the spring of 1951 this shortage of films, and the position of all those who use them, has been deplorable. An agreement between the manufacturers has just been reached by which an allocation is to be made to hospitals according to previous consumption. A radiologist in private practice will receive a percentage of his "usage" which will leave him with time to devote to his hobbies. Clearly an *x*-ray department would have difficulty in maintaining an efficient service on approximately 40% of its film supply, and the cuts at some hospitals may approach this.

The manufacturers say that the various theories which have been advanced to account for the failure to supply films are untrue. It is denied that there has been any faulty distribution, shortage of raw materials, or stock piling, and that closing the factories for a fortnight in the summer or an increased export accounts for the position. The official figures for exported film which has passed through the customs during the eleven months January–November in each year are 7,591,000 sq. ft. (1949); 8,632,000 sq. ft. (1950), and 13,997,000 sq. ft. (1951). An average large teaching hospital uses about 130,000 sq. ft. of film in a year. The film exported in June, 1951, alone was 3,746,000 sq. ft. and would have met the needs of 28 teaching hospitals for a year. The manufacturers and the Ministry imply that the root cause is "increasing usage," and the ministerial letter continues with advice on economy. This advice strikes a nice balance between needs and risks.

A praiseworthy act of the Ministry in the early days of the National Health Service was to develop the *x*-ray services and to install much new plant. In the last two years there have been established or added 560 major units in various clinics. These centres do not work with mass miniature apparatus but use the standard large film.

The committee of every hospital in the country has probably discussed the expense of its *x*-ray department and methods of reducing it. In the summer of 1951 an earnest attempt was made by most hospitals to economize. The long examinations for the kidney, gall-bladder, and intestinal tract were curtailed, with a decrease in efficiency and with little saving in annual expenditure because the number of patients was rising. Within recent years many radiographic techniques have changed and new methods have been evolved, particularly for the skull, chest, and vascular system. None saves films, except mass miniature radiography. Tomography is a most expensive addition. In the absence of expert supervision a physician may be presented with six or more large tomograms which may fail to delineate the lesion either because the "cut" is at the wrong level or the radiographer has made an error in exposure. In addition the usefulness of the tomogram is not understood by many clinicians, and the examination is often requested for lesions which an experienced radiologist would know to be unsuitable.

The consumption of *x*-ray films in hospitals and clinics is difficult to limit, particularly in large departments which strive for a high standard. Wastage occurs each winter by a variation in power at peak hours which disorganizes the exposure charts of every radiographer. Films are wasted by the duplication of examinations in out-patients and wards, by requesting films of both knees when one is affected, by ordering postero-anterior and lateral films of the chest before the former film has been inspected. These are obvious but common mistakes. Equally appreciated is the zealous houseman who tries to anticipate every wish of his consultant. The arrival of a new batch of medical officers is reflected in an increase in the work of auxiliary departments, but this increase is temporary.

The staggering demand made on manufacturers of film has increased progressively in the last few years in spite of instructions to the junior medical staff and restrictions on their privilege. Fortunately the graph of consumption shows some sign of check in its rapid ascent. It is safe to say that further economy in *x*-ray departments will be very difficult to obtain,

[1] *British Medical Journal Supplement*, 1951, **2**, 255.

because so much effort has already been made and because demands on these departments will not be less. A great saving in film, measured by the thousand square feet, could be made by wider use of miniature film, particularly in chest clinics. The experts at the Ministry are aware of this fact and have been engaged during the last six months testing various types of apparatus and films.

Apart from radiology, photographic film serves many functions—in industry, entertainment, and pleasant recreation. It would not be difficult in a welfare state to place these items in an order of importance and priority. This has not been done. Hope for the future rests on an increased production, which is promised in the summer, but this expectation is denied by a shortage of silver, which is also promised.

The components of *x*-ray film are imported from hard currency countries, and one explanation for the position is that it is necessary to maintain and even increase the export of films as part of the general effort to survive beyond the present period of financial difficulty. If this is the position a statement of the facts as they refer to *x*-ray films would be timely and well received. It would procure greater and more enduring economy in hospitals than any other method. As one radiologist has said, "Should we have food for the fit or films for the failing?" It is a difficult question to answer.

TESTS OF RESPIRATORY FUNCTION

Those who study the more chronic diseases of the lungs have for long felt the need for a measure of respiratory function. Skiagrams give little indication of the degrees of disability. Thus in welder's siderosis the radiological changes are gross and the disability is slight, while the reverse holds for asbestosis. Similarly byssinosis causes extreme shortness of breath and early death without giving rise to any shadows on the *x*-ray film which could be regarded as specific. If some satisfactory method of studying the efficiency of respiration could be devised it might prove useful in indicating that damage was being done to the lungs of workers exposed to dangerous dusts before radiological evidence was forthcoming. Unfortunately, no test has so far proved ideal, partly because they are nearly all under voluntary control and thus dependent on the co-operation of the patient. The degree of this co-operation can never be estimated accurately, as has been shown by D'Silva and Mendel,[1] who compared results obtained in a student group giving full co-operation with those obtained in a similar control group of hospital patients not suffering from lung diseases. The difficulty applies particularly to the simple tests, such as chest measurement, exercise tolerance, and vital capacity, which up to the present have been most used. As a result many new methods have been developed. The maximum breathing capacity, a test introduced by Hermannsen[2] in 1933 and developed in recent years by Couma,[3] Wright,[4] and Gilson and Hugh-Jones,[5] is estimated by getting the patient to breathe as deeply and fast as he can while the volume of air moved per minute is measured. This test has not proved very satisfactory, since it is still under voluntary control, and D'Silva and Mendel have shown that an apparatus error, inherent in all spirometers, and which cannot easily be allowed for, becomes important at high respiratory rates. Donald[6] found that patients with emphysema showed an impaired reaction to the inhalation of 4% carbon dioxide, and he therefore investigated the effect of this on 56 coal-miners with pneumoconiosis, in the hope that this test would throw some light on their disability. The results, however, were disappointing, for five subjects who had severe dyspnoea on the slightest exertion, as well as massive shadows on their *x*-ray films, reacted normally to carbon dioxide. In fact impaired reactions were found only in those who had considerable emphysema.

Motley, Lang, and Gordon[7] carried out measurements on 100 miners with pulmonary symptoms and a long history of exposure to coal dust. They found that the residual air expressed as a percentage of the total lung volume was not significantly increased in a third of the cases. They suggest that the disability arises from fibrosis and the unequal alveolar aeration and perfusion, with consequent decrease in the amount of oxygen in the arterial blood. It is of course evident that the function of the lung is to oxygenate the blood, and that the amount of oxygen in the arterial blood can be a valuable guide to the efficiency of lung function. The range of reading between saturation and unsaturation is, however, very narrow, but this can be widened if the oxygen tension is altered. Motley and his colleagues found that a decrease in the saturation of oxygen in arterial blood after exercise was a significant finding in the assessment of disability. The resting arterial oxygen saturation alone was poorly correlated with impairment of pulmonary function, since the measurements of the exchange of respiratory gases might be normal at rest although grossly abnormal during exercise. In another review of the subject Motley[8] suggested that the physiological tests of pulmonary function might be divided into five groups: those that measure lung and ventilation volume, such as vital capacity, maximum breathing capacity, and minute ventilation rate, at rest and during exercise; the residual air expressed quantitatively as a percentage of total lung volume; arterial blood oxygen saturation, at rest and during exercise; the oxygen uptake from inspired air; and increased pulmonary arterial pressure and pulmonary vascular resistance during exercise.

Elsewhere in this issue (p. 65) Dr. P. Hugh-Jones reports a further attempt to devise a simple scientific measure

1 *Thorax*, 1950, **5**, 325.
2 *Z. ges. exp. Med.*, 1933, **90**, 130.
3 *Medicine, Baltimore*, 1948, **27**, 243.
4 *J. thorac. Surg.*, 1949, **18**, 372.
5 *Clin. Sci.*, 1949, **7**, 364.
6 Ibid., 1949, **8**, 45.
7 *Amer. Rev. Tuberc.*, 1950, **61**, 201.
8 *Penn. med. J.*, 1950, **53**, 119.

of exercise tolerance. He has taken the commonly used stepping test, but instead of bothering with pulse rates and respiratory rates or subjective estimates of breathlessness he measures with the aid of an old gas-meter the air volume breathed per minute by the patient during exercise. The exercise is standardized so that it is the same for each patient regardless of his weight, and this is achieved by adjusting the height of the step and the rate of stepping, while the amount of work done in the five-minute test period is not enough to prove distressing.

This test is simple to carry out, requires only such apparatus as an ordinary consulting-room might have, and bears some relation to the activity of daily life. Hyperventilation through nervousness does not produce error owing to the way in which resting ventilation and exercise ventilation are combined in the final results. While the test may be used by itself in following, for instance, the treatment of heart failure, it still has to be combined with other investigations in studying industrial lung disease to separate out the fraction of exertion dyspnoea which is purely pulmonary in origin.

ACUTE INFECTIOUS LYMPHOCYTOSIS

An infectious disease in which recognizable illness is slight or absent and in which almost the only sign may be an excess of lymphocytes in the peripheral blood is not easily diagnosed. It is not surprising, therefore, that since Smith[1] first drew attention to acute infectious lymphocytosis as a clinical entity in 1941 little new knowledge has been added to the subject. Many of the reports have described small institutional outbreaks, and it has been the almost accidental finding of a high lymphocytosis on routine blood examination that has unmasked the "epidemic." The group of six cases reported in this week's issue by Dr. H. G. Dunn belongs to such a category, for all were associated with a nursery in the East End of London, and in four of them there was little reason to suspect a systemic illness. The contrast between infectious lymphocytosis and classical infectious mononucleosis is thus fairly clear-cut. In the latter condition some form of clinical illness is usual —although the signs may be diverse—the lymphocytes are atypical and immature, and heterophile antibody can be found in the blood serum. In acute infectious lymphocytosis, on the other hand, there may be few clinical signs or symptoms, although some cases have been described with gastro-intestinal upset or, as in Smith's early cases, with a mild infection of the upper respiratory tract. The leucocytosis, however, may be out of all proportion to the illness, and, as can be seen in two of Dunn's cases, counts of 70,000 or 80,000 are quite common. Further, unlike infectious mononucleosis, the cells are normal small mature lymphocytes. On these grounds, therefore, the two conditions can be distinguished with reasonable certainty, despite the undoubted fact that all cases of infectious mononucleosis do not strictly conform to the canonical description.

Having said this, however, one must equally firmly assert that the presence of a lymphocytosis should not be regarded as necessarily implying the diagnosis of acute infectious lymphocytosis. Similar cell counts are seen in many other conditions. Pertussis is the most common, and it would be interesting to know whether the usual lymphocytic response is associated with the mild infection caused by *H. parapertussis* or, in the vaccinated child, by *H. pertussis*—illnesses which do not necessarily declare themselves with the characteristic whoop. Mumps, infectious hepatitis, certain stages in the recovery from acute infections, and sensitization itself—all these may induce a lymphocytosis, though, it is true, not usually of the magnitude seen in the infectious variety. It is worth pointing out that, although this condition was first seen only in young children, isolated examples in adults have now been recorded.[2 3] A feature of the adult cases has been that the total white-cell counts have been much lower than those seen in children. The type of cell thus becomes of some importance in distinguishing the condition from infectious mononucleosis.

Five of Dunn's group of cases were associated with *Giardia lamblia* infestation, but it seems unlikely that this could explain such a high lymphocytosis. While Ormiston and his colleagues[4] drew attention to a mild eosinophilia in some of their cases of giardiasis, they made no comment upon lymphocytosis, which could hardly have escaped notice if it had been present. Even so, the observation may be of importance in view of the complete uncertainty about the cause of the condition.

There is always the danger that ignorance may be masked by attaching a convenient diagnostic label to a condition about which there is much uncertainty. It is quite conceivable that acute infectious lymphocytosis should be regarded more as the reaction of the host to a variety of agents than as a specific entity: such a view takes into account the need to consider other manifestations of infection in any epidemiological study. Dunn's investigation raises the possibility that a closer observation of minor bowel upsets in children in institutions and day nurseries might be rewarding.

1 *Amer. J. Dis. Child.*, 1941, **62**, 231.
2 Duncan, P. A., *New Engl. J. Med.*, 1945, **233**, 177.
3 Malamos, B., and Stamatelakis, A., *Lancet*, 1951, **1**, 148.
4 Ormiston, G., Taylor, J., and Wilson, G. S., *British Medical Journal*, 1942, **2**, 151.

EXPERIMENT IN HAITI

Haiti, in the West Indies, the earliest state to be governed constitutionally by negroes, has been the field of a pilot project for reducing illiteracy and encouraging hygiene and social welfare.[1] The project, sponsored by Unesco and the Haitian Government, with the co-operation of the World Health Organization, was started two years ago in the rural area of Marbial, with a population of about 28,000. In this valley all the problems of overpopulation, land hunger, soil erosion, poverty, and declining agriculture were encountered. An anthropo-

1 *The Haiti Pilot Project. Phase One, 1947–49.* Unesco Monographs on Fundamental Education, 1951, Paris. Obtainable from H.M.S.O., London. Price, 2s.

logical survey was first undertaken, and a start was made with an educational programme to bring to the people elementary knowledge and simple skills. During the period of survey famine conditions followed an 11-months' drought, and some adults and children died of starvation; but even in normal years it is said that few of the peasants grow enough to feed their families from one harvest to the next, and they never have enough money to purchase adequate food in the interval. Except in relatively well-to-do families, meat is eaten perhaps only once a month, and fats of any sort are scarce. One of the tasks of the campaign was to teach the peasants to vary their diet, and not to despise such useful foods as grapefruit.

Illness in such a community is, of course, a catastrophe, and there is almost no medical assistance. A private doctor has gone twice a week to Marbial from the near-by town of Jacmel, but few could afford to pay his nominal fee or buy the medicines he prescribed. Malaria is endemic; many of the people suffer from yaws, and hookworm and tropical ulcers are common. There are herb doctors whose treatments are a mixture of common sense and magic and who are fairly skilful in childbirth, massage, and the setting of broken bones; their fees are modest and their intentions at least are good. Those undertaking the survey found a certain open-mindedness on health education. While the peasants often assign supernatural causes to illness and may resort to magic and charms in their search for cures, they do not hesitate to go to a qualified doctor when they can. They accept instruction on bodily and household cleanliness, perhaps out of a concern for prestige rather than for hygiene, but prestige may be a useful motive to play upon.

The early activities of the project have been in the fields of education, agriculture, and development of crafts and rural industries. The plan also provides for the setting up of a clinic and maternity centre, not only to meet the needs of the community for medical services, but to train teachers and workers in health education. The clinic is to be closely associated with the hospital at Jacmel. When a small clinic was opened in September, 1948, it proved almost too successful, for the doctor who came from Jacmel was quite unable to treat all the patients who flocked to him. In virgin areas such as this the approach to preventive medicine must be through curative medicine, which has much more appeal. No large-scale campaign of preventive medicine or sanitary engineering has been started, but energies so far have been directed towards obtaining the active co-operation of the people, so that they themselves can be enlisted in the effort to raise the social level of their community.

BEGINNING TO BREATHE

Recent correspondence in the *Journal*[1 2] has raised once more the question of the limits to our knowledge of the physiology of the newborn infant. From time to time we are all guilty of extrapolating back into neonatal life from the established physiological facts of adult life. We continue to do this in spite of a growing and impressive body of knowledge which shows the infant to have marked functional differences from the adult. We should no more argue from the adult to the baby than we should from the cat to the whale; particular physiological reactions must be tested in the baby itself. Knowledge of the respiration of the newborn infant is a case in point. In spite of many observations and experiments, it is still true to say that the beginning of extrauterine respiration is not fully understood. Huggett[3] in 1927 introduced to this country the technique of caesarean delivery of the foetus into a saline bath with the placental circulation intact. This gives an excellent experimental preparation, and he himself made observations of the foetal respiratory reflexes[4] and was most impressed with the part which joint movements played in stimulating respiratory activity. This work was continued by Sir Joseph Barcroft,[5] and he has left a widely quoted summary of his findings. Nevertheless, it is generally felt by obstetricians and physiologists that the last word has not been said on the subject.

Turning now to the newborn child, we are faced with respiratory behaviour that differs greatly from that of the adult. Gibberd[6] has stressed the part played by extraneous nervous stimuli play in regulating the minute volume of the newborn. However, when the infant sleeps quietly it must surely be dependent for respiratory control upon its visceral reflexes and gaseous equilibrium. Direct observation shows that periodic breathing is common in the healthy full-term infant, and almost universal in the otherwise normal premature infant. In adult life this type of breathing has a serious prognostic significance, or else may be associated with induced hypoxia, as has been so beautifully demonstrated by Haldane.[7] It is no longer thought that the normal infant breathing air is suffering from hypoxia,[8] so that the mechanisms which have been analysed by Haldane are not directly applicable to the baby.

It is only since the introduction of the body plethysmograph[9] that the response of the infant to artificial gas mixtures has begun to be studied in a quantitative manner. Since its introduction the instrument has been modified[10] and it is now possible to have infants sleeping normally in it for long periods. A recent accurate assessment by Cross and Warner[11] of infantile responses to high and low oxygen mixtures suggested the probability that the carotid-body reflex was more active in the newborn infant, and a later incomplete report[12] seems to show even greater activity of the peripheral chemoreceptors in the premature infant. In spite of this active reflex, it appears that no newborn baby has a good defence against prolonged hypoxia, as the medulla seems to become depressed in these circum-

1 Watson, G. I., *British Medical Journal*, 1951, **2**, 417.
2 Bowes, K., ibid., 1951, **2**, 546.
3 *J. Physiol., Lond.*, 1927, **62**, 373.
4 Ibid., 1930, **69**, 144.
5 *Researches on Prenatal Life*, 1946, ch. 22. Blackwell: Oxford.
6 *A Short Textbook of Midwifery*, 1951, 5th ed., ch. 29. J. Churchill: London.
7 *Respiration*, 1935, 2nd ed., p. 68. Clarendon Press: Oxford.
8 Graham, B. D., Reardon, H. S., Wilson, J. L., Tsao, M. U., and Baumann, M. L., *Pediatrics*, 1950, **6**, 55.
9 Deming, J., and Washburn, A. H., *Amer. J. Dis. Child.*, 1935, **49**, 108.
10 Cross, K. W., *J. Physiol., Lond.*, 1949, **109**, 459.
11 Ibid., 1951, **114**, 283.
12 Ibid., 1951, **115**, 17P.
13 *Leçons sur la Physiologie comparée de la Respiration*, 1870. Baillière: Paris.
14 *Pediatrics*, 1948, **1**, 581.

stances. It should be stressed that this work is not yet confirmed. However, it underlines the importance of the baby as an object of separate physiological study.

One factor in the ability of the very young animal to withstand anoxia which deserves mention is its power of anaerobic metabolism. This was shown as long ago as 1870 by Paul Bert,[13] and has been confirmed recently by Wilson and his colleagues.[14] In spite of this the clinician should never rely upon it, and all efforts should be made to obtain normal oxygenation as soon as possible after delivery.

"PRISCOL" IN CEREBRAL ARTERIOSCLEROSIS

The symptoms of cerebral arteriosclerosis which, in the absence of acute episodes such as a cerebral thrombosis or haemorrhage, are probably due to chronic cerebral ischaemia are very resistant to any form of treatment. Vasodilators such as oral nicotinic acid have been used with only occasional success. In a recent issue of this *Journal* (October 13, 1951) Smith and Turton described the use of "priscol" in an arteriosclerotic patient who had severe executive dysphasia and difficulty in writing, together with emotional changes. Although the authors state that there was no evidence of a focal lesion the presence of executive dysphasia and dysgraphia with apparently normal comprehension of spoken speech and of writing suggests strongly that there was in fact focal damage in the left fronto-temporal region, but whether this resulted from a cerebral thrombosis or not is uncertain. The effect of an intravenous injection of 40 mg. priscol was dramatic: within a few minutes there was evidence of vasodilatation in the skin and retinal vessels and remarkable improvement in speech and writing ability. The improvement lasted about three hours, and the patient then relapsed into his original condition. The same effects followed a second injection, while there were no changes after intravenous injections of sterile water or of vitamin B_1. Oral administration of priscol was then tried in a dose of 25 mg. six times a day, and after 48 hours there was again remarkable improvement. Unfortunately the patient's condition gradually returned to its original state in spite of increasing doses.

Priscol (2-benzyl-4,5 imidazoline hydrochloride) has a complicated pharmacological action, but among other effects it has been shown experimentally to cause vasodilatation of the peripheral and coronary vessels,[1] and its effect on the cerebral vessels of the cat is illustrated in a letter on p. 106. In man a similar peripheral vasodilatation has been demonstrated after intravenous injection and to a lesser extent after oral administration.[2] The drug has been used with successful relief of symptoms in peripheral arterial disease, the best results being obtained when there is a large element of spasm as in Raynaud's disease, but improvement in intermittent claudication and in the rest pains of occlusive arterial disease occurs in some patients.[3,4] The question of spasm of cerebral vessels in association with cerebral arteriosclerosis is a debatable one, but in some patients the symptoms suggest that there may be episodes of arterial spasm. Although the action of priscol on the cerebral blood vessels is not known for certain the results in Smith and Turton's patient suggest that vasodilatation occurs, and an extended trial of the drug in suitable patients with cerebral arteriosclerosis would seem to be worth while.

[1] Ahlquist, R. P., Huggins, R. A., and Wordbury, R. A., *J. Pharmacol.*, 1947, **89**, 271.
[2] Grimson, K. S., Reardon, M. J., Marzoni, F. A., and Hendrix, J. P., *Ann. Surg.*, 1948, **127**, 968.
[3] Douthwaite, A. H., and Finnegan, T. R. W., *British Medical Journal*, 1950, **1**, 869.
[4] Goodwin, J. F., and Kaplan, S., *ibid.*, 1951, **1**, 1102.

"M. & B.I."

Medical and Biological Illustration enters its second year with the next number. In spite of the somewhat trying conditions prevailing in 1951, which made it an inauspicious year in which to launch a new publication, and in which cost of paper has risen steeply, the journal seems to have met a definite need, and already it has gained an encouraging readership abroad—principally in the United States.

Casual conversation, however, shows that there are still many working in the fields which the journal covers who have never heard of it. News spreads slowly, and there are so many journals on the library table that to overlook a new one may be forgiven. Seeing the cover only, some may decide that the journal is of a technical nature and therefore of no interest to them. It is true that there are technical articles, but many are general in scope, and are aimed at the user of illustration rather than the producer. The teacher is well served, and a new series covering all aspects of the preparation and publication of a medical book should have a wide appeal. Liberal illustrations make even the technical articles less indigestible for the non-technical user, and simple curiosity may make him aware of new developments without the need to assimilate the actual methods of production: he will often find these applicable to his work, whether clinical, research, or teaching. There are historical papers, too, which have no worrying technicalities. That the subject is growing is shown by the enlargement of the valuable abstract section, and the Association's foresight in sponsoring *Medical and Biological Illustration* is borne out by the news of a new journal, *Via Optica*, which is to appear in the United States. The *Journal of the Biological Photographic Association* is another American publication, but this affords little recognition to the medical artist, while our own journal caters for all branches.

This catholicity of interest is of especial importance in connexion with another event which is to take place at B.M.A. House in June, 1952, when the Medical Group of the Royal Photographic Society and the Medical Artists' Association are presenting a joint exhibition of illustration. This is the first time that the work of the two main branches of medical illustration will be seen together, and it augurs well for the future. Together with *M. & B.I.*, it implies the disappearance of the suspicion with which the painters and the photographers have been prone to regard each other—a suspicion which can only do harm to the wider aims of medical illustration.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE BASIC PRINCIPLES OF ATOMIC STRUCTURE

BY

Sir JAMES WALTON, K.C.V.O., M.S., B.Sc., F.G.A.

Correspondence in the *British Medical Journal* and remarks made to me personally following the two papers on isotopes in medicine published in the *Journal* of September 29 have made it evident that many members of the medical profession have difficulty in understanding modern atomic physics. This is very understandable when it is realized how recent is the growth of this subject, so that there must be many general practitioners and specialists who learnt their physics in the days when an atom was only an atom. Now it is becoming essential that, with the progress of medical treatment, they should have an elementary knowledge of the underlying principles of atomic structure. The literature is, however, so immense and the many textbooks are often so large and highly technical that general practitioners have neither the time nor the opportunity to study them. It is my belief, nevertheless, that by omitting all mathematical considerations and the lines of reasoning that have led to the conclusions, and by concentrating upon the actual experimental findings and the accepted results, an elementary knowledge of the facts can be given very simply and briefly. It is true that such a method tends to be too dogmatic, in that certain conclusions which are still under discussion, or even not accepted by many, have to be stated as facts, but this is a privilege which is granted to all elementary teachers and may not be unduly harmful.

The Atomic Theory

About 500 years B.C. the Greek philosopher Leucippus taught that the ultimate constituents of all things were empty space and atoms, which were infinite in number, indivisible, and always in motion. About 100 years later Democritus, who is usually credited with the atomic theory, developed this view and taught that atoms were the ultimate material of all things and, although not visible, were heavy and impenetrable. These views, which were purely theoretical, were forgotten for some 2,200 years, when in 1804 Dalton announced his famous atomic theory, in which he showed that atoms could be defined as the smallest particles in which an element can exist, that they could not be broken up by chemical means, and that they possessed definite weights which could be expressed by numbers relative to the atomic weight of hydrogen, which is the lightest known element. Alternatively, they could be defined as the smallest part of an element which could enter into chemical combination with another element.

In 1864 John Newlands showed that if the elements were arranged in the order of their atomic weights there was a recurrence of similar chemical and physical characters at every eighth element. This he described as the "law of octaves." In 1869 Mendeléeff developed this idea more fully and published a table with the elements arranged according to his periodic law. Since then many new elements have been discovered, and their insertion in the position of the table indicated by their atomic weights has confirmed his views and fulfilled his predictions.

Structure of Atoms

In 1897 Sir J. J. Thomson found that by passing an electric current through a glass tube filled with an attenuated gas of any variety (Fig. 1) a luminous ray was given off in a straight line from the cathode. This cathode

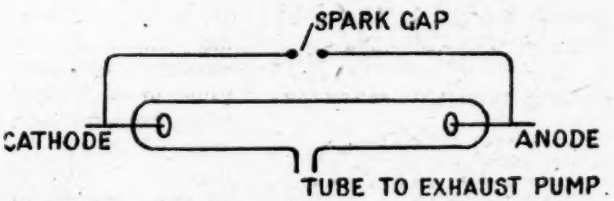


FIG. 1.—Sir J. J. Thomson's apparatus for generating cathode rays.

ray could be deflected by electric and magnetic fields in a direction showing that it was made up of negatively charged particles which are known as *electrons*. They have a speed of approximately 1/10 that of light, produce luminescence when they impinge on certain substances, cause the leaves of an electroscope to diverge, and have considerable penetrating powers. Since they come from any gas, they must be a constituent of all atoms. The electrical charge which each electron carries is taken as the unit charge. They have been estimated to have a diameter of only 10^{-5} of a hydrogen atom and to weigh only 1/1,840 of its nucleus.

The fact that negative particles are obtainable from atoms suggested that similar positive particles must be present, as atoms are electrically neutral. Goldstein was able to demonstrate their presence, and in 1898 Wren proved that they were positively charged. Mosely was able to show, by *x*-ray spectroscopy, the actual number of these particles, which are known as *protons* and are grouped together to form a *nucleus*. Since each contains a unit positive charge and the total atom is neutral, they must equal the number of electrons. Their number in each atom is known as the *atomic number* of that atom. They weigh approximately 1,840 times the weight of an electron. It is the number of the protons which determines the nature of the element. In hydrogen there is only one, in helium two, and so up the scale to uranium with 92. If the number of protons is altered, as occurs naturally in radioactive substances or can be brought about artificially, the element is changed to another.

The fact that the atomic number is less than the atomic weight, except in the case of hydrogen, made it evident that other heavy particles must be present, and in 1931 Sir James Chadwick discovered the presence of *neutrons*, which are in the nucleus and have a like weight to the protons, they and the protons forming nearly the whole of the weight of the atom. Neutrons have,

however, no electric charge, and their presence therefore does not affect the number of electrons and the chemical properties. They steadily increase in number with the atomic number but not in the same ratio; deuterium, or "heavy hydrogen," contains one, helium two, bromine 45, and uranium 146. Together with the protons they give the atomic weight of the element.

In 1885 a Swiss schoolmaster named Balmer discovered that there was a definite mathematical relationship between the positions of the lines seen in the spectrum of the light from glowing hydrogen. Based largely upon this knowledge and upon the later brilliant work of the late H. G. J. Mosely on the wavelengths of the *x*-ray spectra of the elements, the Danish physicist Niels Bohr was able in 1913 to evolve his famous model of the atom. He showed that it consisted of a heavy central nucleus around which the electrons moved in ellipses in any plane; the ellipses formed shells placed at distances corresponding to the square numbers 4, 9, 16, 25, 36, etc., from the nucleus, the numbers of electrons in each shell being fixed for each atom. Hence by far the greater part of an atom consists of empty space. In hydrogen there is only one shell containing one electron, but on passing down the periodic table the numbers gradually increase (Fig. 2), the number in the individual shells being 2, 8, 18, 32, 18, 12, 2, this being the arrangement of electrons found in uranium, the heaviest known element. Generally speaking the electrons are more loosely attached in the outer shells, so that the inner shells are filled first. The total number of electrons corresponds to the atomic number. The outer electrons are those which are concerned in chemical reactions, and it is found that those elements which have similar chemical characters—that is, which are in the same columns of the periodic table—have a similar number of electrons in their outer shells, thus confirming Mendeléeff's views in a remarkable manner.

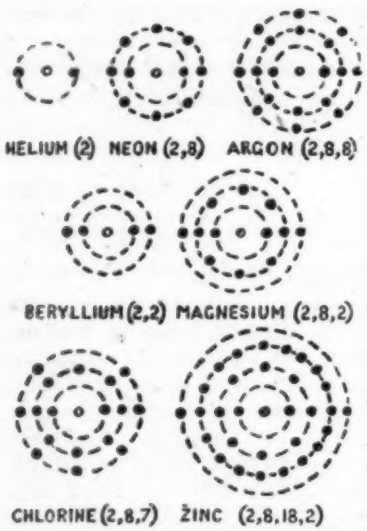


FIG. 2.—Diagrams showing the arrangement of the electrons in atoms of helium, neon, argon, beryllium, magnesium, chlorine, and zinc. The diagrams are purely schematic: the orbits or shells are much further apart, and they are in the form of ellipses, not circles; also they may lie in any plane.

Ionization and Electrolytes

Electrons may be displaced from the outer shell of an atom, and, being free, will soon become attached to other atoms of a similar or different nature. The atom from which an electron has been displaced will have lost one unit negative charge and hence will be positively charged. It is known as a *positive ion*, or, since it is attracted to the cathode, as a *cation*. In the same way the atom which has gained an electron is negatively charged and is known as a *negative ion*, or, since it is attracted to the anode, as an *anion*. Certain simple salts when dissolved in water separate into ions, when they are known as *electrolytes*, and, as Faraday showed early in the nineteenth century, can be separated by the passage of an electric current, a process known as *electrolysis*. The passage of a high potential electric charge or of rapidly moving atomic particles through a gas will knock off electrons, causing the gas to become ionized and to become an electrical conductor. Certain resins have the power of attracting different ions and thus bringing about their separation. This process is to-day largely used commercially, but it has also its medical application (ion-exchange resins).

Isotopes

It had long been known that certain elements showed varieties which, although identical in every chemical and in most physical characters, had different atomic weights: for example, when uranium breaks down completely it is converted into lead of atomic weight 206. The actinium series in breaking down ends as lead with the atomic weight 207, and that derived from thorium has an atomic weight of 208, but all three are lead in every sense of the word. To these elements Soddy in 1913 gave the name *isotopes*. The differences in the

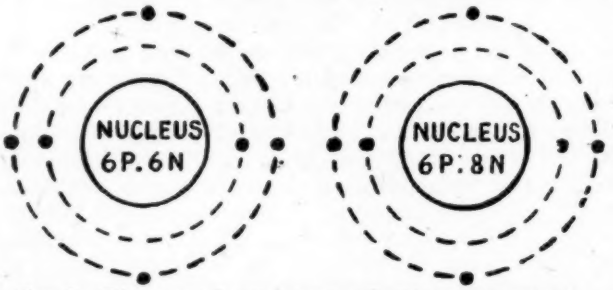


FIG. 3.—Diagrams of two isotopes of carbon, C^{12} and C^{14}.

atomic weights are due to the number of neutrons, and, since they have no charge, the number of electrons and hence the chemical characters are unchanged. Mass spectrography has shown that the majority of elements have isotopes (Fig. 3), and the fact that many atomic weights are not whole numbers—for example, magnesium 24.32, chlorine 35.457, tin 118.70—is known to be because they are mixtures of isotopes with different atomic weights. The nature of the isotope is usually shown by an index number giving its atomic weight—for example, C^{11}, C^{12}, C^{13} of carbon, or P^{31}, P^{32} of phosphorus. Sometimes the atomic number is also indicated—for example, ${}^{11}_{6}C$, ${}^{13}_{6}C$, or ${}^{31}_{15}P$, ${}^{32}_{15}P$. One isotope of hydrogen is of double the atomic weight owing to the presence of a neutron in the nucleus: it is known as deuterium, and its nucleus as a *deuteron*; a still heavier isotope is tritium, with two neutrons and an atomic weight of three.

What Prevents Spontaneous Atomic Explosion?

Physicists had long been puzzled over why the protons in the nucleus did not repel one another and the atom spontaneously explode. In 1934 Yukawa suggested that negatively charged particles would be found within the nucleus. They have since been discovered and are known as μ *mesons*. They have a unit negative charge like an electron and a mass between that of an electron and a proton. There are probably at least four varieties having from 200 to 1,000 times the weight of an electron. They are produced naturally by cosmic rays in the upper air,

are capable of penetrating 20 ft. (6 m.) of lead, and have only a short existence. They were believed to bind together the protons by a reaction known as exchange attraction, which occurs only in minute structures of atomic dimensions, so that if once the protons are separated by a short distance they repel one another with great force and the atom is disrupted. Later work (*vide* Sir John Cockcroft, *Nature*, 1951, **168**, 1060) has shown that the Yukawa hypothesis is no longer tenable, as the μ mesons discovered by Anderson and Neddermeyer scarcely interact with nuclei, and in 1947 Powell discovered the π meson or pion, which may be positively charged, negatively charged, or neutral, the positively charged meson $\pi+$ having a very short life (10^{-8} of a second) and changing into a μ meson. They have a mass about 275 times that of an electron. There is also evidence that there are even other and heavier mesons.

In 1932 Anderson and Blackett discovered yet another particle which is produced when cosmic rays are stopped by collision with a metal plate. These particles were found to be positively charged and were called *positrons*. They have since been obtained by bombarding aluminium with α rays, or lead with γ rays (see definitions below). They have a mass approximately that of an electron. They are probably formed by the nucleus absorbing the energy of a γ ray and converting it into a positron and an electron. The life of a positron is very short—about 10^{-9} seconds in the air. It then disappears completely, probably by combining with another electron and being entirely converted into energy as a γ ray, thus supporting Einstein's contention that energy and matter are interchangeable.

An atom therefore consists of a compact nucleus in which is centred by far the greater weight and which contains positively charged protons and positrons, negatively charged mesons, and neutrons with no charge. The number of protons determines the nature of the element, and the combined weight of the protons and neutrons gives the atomic weight. Surrounding the nucleus at relatively great distances are a number of electrons, corresponding to the number of protons, moving in various planes in definitely placed elliptical shells around the nucleus. They are concerned with chemical changes only. The smaller atoms are estimated to be about 2×10^{-8} to 6×10^{-8} of a centimetre in diameter and the electron to be only 10^{-5} of the diameter of the atom of hydrogen in its normal state.

Radioactivity

In 1896, a year after Roentgen discovered x rays, Becquerel showed that a uranium salt gave off rays capable of affecting photographic plates. Further investigation has shown that these rays are of three sorts.

α Rays.—These are composed of the nuclei of helium—that is, of packets of two protons and two neutrons moving at great speed (2×10^9 cm. a second). They therefore contain two unit-positive charges but are deflected with difficulty. Because of their small mass they have but little penetrating power, but because of their high speed they tend to break up atoms in their path, leaving free ions and so ionizing the air.

β Rays.—These are electrons moving at prodigious speeds. They are easily deflected and are 100 times more penetrating than α rays.

γ Rays.—These are identical with x rays, and consist of electromagnetic waves with no mass. They have very short wavelengths; about 0.005 A, are extremely penetrating, and cause slight ionization, photographic, and fluorescent effects.

In searching for the source of these rays, the two Curies in 1898 extracted from pitchblende a number of radioactive substances, including radium, the most active of all. In 1902 Lord Rutherford showed that the emission of the rays was due to atomic disintegration, and that the seat of instability was the nucleus. It is the heavier atoms which show radioactivity, and it is present in all atoms with a higher atomic weight than bismuth. It would seem that nuclei containing large numbers of protons and neutrons are unstable. It is possible, therefore, that in the past there were elements of a higher atomic weight than those now known, but that they have completely degenerated.

Transmutation of Elements

In 1919 Rutherford exposed nitrogen to radium so that it was bombarded with α rays, and was able to convert some of the nitrogen into O^{17}, an isotope of oxygen, thus:

$$N^{14} + He^4 = O^{17} + H^1$$

In 1932 Cockcroft and Walton were able to accelerate protons by very high voltages, and by their use were able to convert an isotope of lithium, Li^7, into two α particles, thus:

$$Li^7 + H^{1.0078} = H^4 + H^4 + \text{energy}.$$

By bombarding the isotope Li^6 with deuterons, a similar result was obtained:

$$Li^6 + H^{2.0156} = H^4 + H^4 + \text{energy},$$

but if Li^7 was bombarded with deuterons a neutron was also produced. It is reactions of this sort which are the basis of the hydrogen bomb. To-day large numbers of rapidly moving charged particles may be directed upon elements by the use of the cyclotron. This is a large and powerful machine consisting essentially of two electrodes for producing ions, and a high-frequency oscillating electromagnetic field for repeatedly accelerating the ions as they travel in an ever-widening flat spiral. After about a hundred revolutions the ions are drawn off their spiral track into a bombardment chamber, where they may be used to produce neutrons or electrically charged particles such as protons, mesons, and, to a lesser degree, electrons The neutrons can be used to make radioactive isotopes artificially, but this is usually now done in an atomic pile (see below).

By these means, elements may be bombarded with protons, α particles, deuterons, or neutrons. When protons meet other nuclei the result will depend upon their energy resonance. If less than that of the nucleus they will bound off. If of similar resonance they will enter it and form a new element of greater atomic weight In this way two new elements—neptunium and plutonium, both of atomic weight 239 but with atomic numbers of 93 and 94—have been formed. If of a higher resonance they will split up the nucleus, often with explosive force. Neutrons have similar effects, but if they enter the nucleus they form not new elements but isotopes, many of which are unstable and radioactive.

The Chain Reaction

The explosive effect of these bombardments may occur naturally, as in U^{235}. Here protons and neutrons driven off from one atom will explode the next atom, the so-called chain reaction. If the mass is sufficiently large (critical mass) to prevent the escape of the protons and neutrons the whole mass will explode with enormous violence and heat, as in the atomic bomb. The chain

reaction may be controlled, and the enormous energy utilized, by slowing down the protons and neutrons by passing them through material of low atomic weight, such as deuterium or graphite. This is the basis of the *atomic pile.*

Isotopes in Medicine

The isotopes prepared by these methods now number over 700, and, since many are radioactive, they are being used to an increasing degree in medicine. They are used either for treatment, by giving a radioactive element which may have a therapeutic effect, as upon a cancer with an affinity for the element—for example, the isotopes of iodine, I^{128} or I^{131}, for the treatment of some varieties of carcinoma of the thyroid—or to trace the metabolism of an element (or a compound containing it) in the body—for example, phosphorus by its isotope P^{32}. Their use may, however, be associated with danger, for, if their breaking-down period is long, the radioactivity may be carcinogenic rather than curative. Fortunately in the artificial isotopes the period to half-way disintegration (half-life) is usually short; according

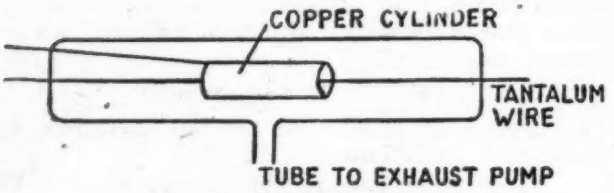


FIG. 4.—Diagram of a Geiger counter.

to Wormall, for the isotopes of iodine and phosphorus it is 8 and 13 days and 14.3 days respectively. This is in marked contrast with uranium, for which it is about 500 million years.

The position in which the isotope is concentrated can be readily determined, if it is radioactive, by the use of the *Geiger counter* (Fig. 4). This consists essentially of a glass tube down the centre of which passes a fine tantalum wire. The centre of the wire is surrounded by a cylinder of thin copper, and the tube contains gas under a reduced pressure, usually argon and ethyl alcohol. The wire is positively charged and the cylinder negatively charged, with a maintained difference of potential such that a discharge will just not pass between them. If a fast-moving electron, proton, α particle, or even a photon of light passes between them, the gas is ionized and a momentary current will pass between the tantalum and copper. This minute rush of current is amplified by radio methods and emitted by a loudspeaker so that it is audible to a number of people standing around. The number of cracks or thumps may be counted or automatically recorded so that the radioactivity can be estimated. Saunders states that the instrument is so delicate that a match lit on the other side of the room gives a rush of such cracks.

"Music while you work" was one of the successful British ideas of wartime which was exported across the Atlantic. In one New York insurance company, employing thousands of clerks and machine operators, efficiency has been raised 19% since the provision of music over the hum of routine work. In department stores suitable music will make the customer linger at the cosmetic or hosiery counter and make a further purchase. And now dentists are offering patients music by headphone to distract them from the noise and vibration of the drill, while those undergoing plastic surgery under local analgesia are also thus diverted.

Reports of Societies

CORTISONE AND A.C.T.H. IN GENERAL PRACTICE

A meeting of the General Practice Section of the Royal Society of Medicine was held at No. 1, Wimpole Street, on December 19, 1951.

Dr. A. TALBOT ROGERS, who opened the discussion on "The Possible Future Use of Cortisone and A.C.T.H. in General Practice," described himself as a general practitioner with a special interest in rheumatic diseases. Being in charge of the physical medicine department of his local hospital, he had had the advantage of co-operating with Dr. E. N. Allott in his work on cortisone and A.C.T.H. (adrenocorticotrophic hormone) at Lewisham. He wanted to emphasize the words *possible* and *future* in the title of the discussion because he felt that there was not much hope that these substances would become widely available in the near future or that the cost of maintaining a rheumatic patient on either of them would soon be diminished from the present level of £10 to £20 a month. Because of this it was right that the supply of cortisone and A.C.T.H. should be limited to research centres; yet general practitioners should know about this type of treatment, as they would be responsible for sending the right type of patient for treatment and for helping to maintain treatment after discharge.

In a brief review of the scientific background of the subject Dr. Talbot Rogers recalled that the pituitary gland was under nervous control and when stimulated by bodily stress released varying amounts of A.C.T.H.; this in turn stimulated the adrenal cortex to produce its many hormones affecting salt and water metabolism, sugar and glycogen, protein metabolism and androgenic activity, in addition to cortisone. The diseases in which A.C.T.H. and cortisone could be used included rheumatoid arthritis and Still's disease: in these two diseases they offered the first really spectacular advance in therapy. In spondylitis deformans he had not experienced such a well-marked response, and, although this had been claimed by some American workers, he felt that this discrepancy was due to disagreement on what constituted spondylitis deformans. Of their activity in rheumatic fever he gave a guarded account, saying that, although they abolished symptoms and seemed to protect the heart, their effect was not yet certain. However, this was an excellent short-term use for cortisone, because the disease process eventually died out and indefinite maintenance doses were not necessary. Other diseases that benefited were acute lupus erythematosus, status asthmaticus, some cases of haemolytic anaemia, periarteritis nodosa, many eye conditions, exfoliative dermatitis, pemphigus, severe burns, and ulcerative colitis.

The Dangers

It was important that the general practitioner should know the complications that might arise from treatment with cortisone or A.C.T.H. The greatest danger with both was that they delayed healing, a serious matter with peptic ulcer or with active or recent pulmonary tuberculosis; septic conditions were masked and tended to spread silently without the usual pain and reddening—they could be detected only by increased swelling and a general rise of temperature. Because A.C.T.H. produced a general secretion of cortical hormones it was liable to produce disturbances in salt and water metabolism, with rise of blood pressure which was particularly dangerous in patients with heart disease. Diabetes could be precipitated and diverse psychotic changes could result—euphoria proceeding to mania or depression and insomnia. Cushing's syndrome was also liable to appear, with the characteristic "moon-face," hirsutism, amenorrhoea, acne, ecchymoses, flattening of the neck, and humping of the back and abdomen with deposits of fat.

In this country both drugs were usually given by injection; this, he felt, was a good thing, because one could seldom trust the patient to take the drug by mouth as regularly as seemed necessary for maintenance. Withdrawal symptoms were serious, and slight changes in the regularity of dosage, especially with A.C.T.H., might well produce serious symptoms. The supplies were so low to-day that the criterion by which the patient should be treated should be his ability to move and work and not be a burden on his family rather than the state of his joints, which, at a dosage graded to keep him at work and avoid complications, might still give pain.

Dr. W. S. C. COPEMAN said that Kendall had isolated 26 different steroid substances from the adrenal cortex, one of which was cortisone. The administration of A.C.T.H. to a patient stimulated the production of all 26, and more side-effects might therefore be expected than after cortisone alone. Although the disease process of rheumatoid arthritis and Still's disease could temporarily be completely reversed, these drugs did not produce a cure, and the patient generally relapsed to his previous condition when treatment was discontinued. In diseases of the eye there was scope for short-term therapy, and in status asthmaticus a single treatment could be life-saving.

Selection of Cases for Treatment

The supply of cortisone might well increase in the near future; at the moment the drug was partially synthesized from ox-bile as a starting product. Another starting product derived from vegetable sources was being investigated, but, although if successful the new process would make cortisone more plentiful, it was unlikely to become appreciably cheaper owing to the complexity of the process involved. Although some patients were able to get a limited supply for themselves from abroad, he was never prepared to treat any that had less than a six months' supply: the mental effect of reverting to their original condition after a short space of freedom was so grave as not to justify a short period of treatment without there being some special reason for this.

Patients suitable for treatment should be selected carefully. The unstable personality was liable to develop a psychosis, and the patient with permanently damaged or ankylosed joints could not expect relief. It did not seem to be necessarily the early case that yielded the best result, since such cases might be at their most active stage and require heavy and prolonged dosage; an old-established case without excessive joint damage often responded better, and might go into remission. The cardiac and the hypertensive patient were unsuitable and renal disease was a contraindication. He had seen one case of insulin-resistant diabetes develop. Gastric ulcers could perforate and herniae strangulate silently without marked symptoms or signs.

Treatment should always be started in hospital, where the patient's characteristics of weight, blood pressure, and water balance should be established and the blood count (especially the eosinophils) and sedimentation rate recorded. The electrocardiograph was useful as a guide to potassium loss, since the blood level was sometimes fallacious. When the patient then returned to the care of the general practitioner the complications that Dr. Talbot Rogers had outlined should be looked for, and also undue fatigue, alkalosis, and osteoporosis, which might be the cause of spontaneous fractures. In patients under treatment pains in bones and joints were probably more often caused by their unaccustomed use than by insufficient control of the disease, and seldom called for increased dosage. To avoid withdrawal symptoms the dose should always be decreased very slowly indeed.

Clinical Results

Of the series of 20 patients with rheumatoid arthritis that Dr. Copeman and his group had selected, in conjunction with the Medical Research Council, for testing the long-term activity of cortisone, after nine months 17 were comfortable and all the men were at work and most of the women doing part-time housework. Only one case had gone into remission; one had developed symptoms of toxicity, and his treatment had been discontinued but later resumed without further ill effects. Dr. Copeman said that cortisone and A.C.T.H. were not a cure for rheumatoid arthritis and had in no way superseded the older methods of treating the disease. They were, however, an important adjunct to treatment in certain cases; above all they were potent "research tools."

Dr. E. N. ALLOTT said that the group of workers at Lewisham was trying to find the minimum doses necessary for treating and maintaining patients. Such was the expense of cortisone that, although an expenditure of £75 to £100 a year might be sufficient in some cases to keep a patient at work, £150 to £200 would often be needed to keep him free of pain and discomfort. Half their supplies had to be set aside for maintaining old patients, and that greatly limited the number of new cases they could take on. Besides the rheumatic diseases, disseminated lupus erythematosus and discoid lupus of the skin had shown great improvement, but both had required maintenance treatment. Polyarteritis nodosa had not responded well; that might be due to insufficiently early diagnosis. One case of scleroderma had made a slight improvement. Two cases of asthma and four of burns had responded well. Cases of leukaemia, agranulocytosis, aplastic anaemia, and nephrosis had not been affected. The results in haemolytic anaemias were hard to assess, but one case of refractory macrocytic anaemia had been improved and had not required maintenance treatment. A case of exfoliative dermatitis had responded well at first, but the disease had become resistant although a gross Cushing's syndrome had been produced by the treatment.

Laboratory Control of Treatment

Cortisone could be given by mouth or by injection every other day or every three days. A.C.T.H. had usually to be given four times a day; the effect of the same amount of material was increased if given more frequently. Of the laboratory tests for controlling treatment, the eosinophil test was unreliable. The blood sedimentation rate was of little value, because only when full doses were given was it decreased; with maintenance doses of the usual size it generally remained as high as in the active disease. 17-ketosteroid excretion was of little use, and blood electrolyte determinations were of limited value. The best control was general clinical observation; electrocardiography was useful for detecting potassium deficiency.

More Clinical Results

Dr. D. BRIGGS (American Hospital of Paris, Neuilly-sur-Seine, France) gave his experience of patients whose treatment was determined by their ability to pay for the drugs rather than by whether they were suitable for treatment; these included nine cases of rheumatoid arthritis. All had responded to cortisone, but one deteriorated with A.C.T.H. One case of Reiter's syndrome had been treated for two months when remission occurred. Cases of status asthmaticus had been cured, but when pulmonary fibrosis formed the basis of the asthmatic condition there had been no response. Various other cases were described. As side-effects he had observed the formation of abscesses in two patients; one of these patients had become drowsy on withdrawal of the drug, and this had been ascribed to sodium loss.

Status Asthmaticus

Dr. K. ROBERTSON (Southampton) confirmed the experience of other speakers about the usefulness of cortisone in status asthmaticus, considerable remissions following one or two doses given during the acute emergency. He hoped that cortisone would be made available for the use of general practitioners faced by that most troublesome and alarming syndrome. He referred too to a dramatic response to cortisone in a colleague with a very severe allergic reaction to

the experimental injection of a staphylococcal antigen, and reported immediate resolution of severe stomal ulceration when A.C.T.H. was given by the slow intravenous drip method. In a case of chronic lymphatic leukaemia, cortisone by mouth had on two occasions produced a striking reduction in size of the enlarged lymph nodes and spleen, though the blood picture had not been influenced. In two cases of what appeared to be irreversible peripheral failure in diabetic acidosis, following the control of hyperglycaemia and biochemical correction of electrolyte disturbance, cortisone had appeared to be life-saving.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Malaria

SIR,—I was much interested in the letters of Colonel L. W. Harrison and Sir Philip Manson-Bahr (December 8, 1951, pp. 1402–3). For anyone to apply to the former the epithet "has been," which he fancied he invited, is merely to emphasize the ignorance of the applier; while the authority of the latter on all questions of tropical and sub-tropical diseases is unchallenged. It is therefore with no little reluctance that I venture to differ from each of them.

In the first place I do not think that the life-saving properties of quinine by injection can seriously be doubted: it is the method of injection which is open to challenge. A long time has passed since the unfortunate "tetanus episode" reported by Semple as a sequel to the intramuscular injection of quinine; and in modern conditions, in the Indian subcontinent at any rate, this sequela should no longer be a bogy. Injectable quinine solutions have long been marketed by many reputable pharmaceutical firms in ampoule form, and these form part of the stock of the great majority even of outlying dispensaries in India, while hospitals of any size are equipped with autoclaves, which should effectively deal with any tetanus spores if it were found necessary to prepare a home-made solution.

The objection—and I venture to think a very valid one—to the intramuscular injection of quinine rests nowadays not on the fear of tetanus but on the confirmed observations of Acton and Chopra (*Indian J. Med. Res.*, 1924, **12**, 251), Karamchandani (*Rec. Mal. Surv. Ind.*, 1933, **3**, 445) and others, that necrosis of the tissues invariably accompanies this procedure. This objection, however, is not applicable to the intravenous injection of the drug; and, this being the case, there would appear to be little or no justification for the selection of the intramuscular route in cases—and they form the great majority—in which the vein is accessible and in which parenteral administration is called for as a life-saving measure. There are, of course, exceptions such as stout women with small veins, and infants and young children, but even in these cases diligent search will often reveal an accessible vein. Accordingly, it was my personal practice in any hospital of which I was in charge to prohibit the intramuscular injection of quinine except in those cases which I or, in my absence, my locumtenent personally sanctioned; and I venture to think that such a course has much to be said for it.

It is to be remembered that the vast majority of cases of malaria are treated not by eminent specialists but by medical subordinates who cannot be expected to have the experience, judgment, or responsibility of the pundits. The effect of the authoritative blessing of the intramuscular route has, to my knowledge, been to encourage the lazy practitioner who is averse from taking the trouble to ensure the proper administration and retention of quinine by the mouth and indulges instead in pincushion therapeutics. Anyone who has seen for himself the crop of painful nodules persisting for months and years resulting from this lazy and pernicious practice cannot fail to have strong views. In one case which I have been able to follow nodules and pain have now persisted for over 10 years. For this reason alone the supersession of quinine by the synthetic antimalarials for oral administration is devoutly to be welcomed.—I am, etc.,

Commonwealth Relations Office, S.W.1. J. B. HANCE.

Humid Climate and Respiratory Diseases

SIR,—I shall be grateful if you will grant me space in your columns to remark on the view, which appears to be held by many doctors, that a warm, humid climate is beneficial to those suffering from respiratory diseases.

For the last five years I have experienced the pleasures and frustrations of practising medicine in Nassau, in the Bahamas. During my first winter here the incidence of respiratory affections, notably asthma, struck me as being excessive. In the following spring and summer I made the same observation concerning hay fever. Later experience here has confirmed both observations. The increased incidence of these affections appears to be directly related to the excessive humidity of the climate, which averages between 70–80% in the winter months and between 80–90% in the summer months. Occasionally during winter a relatively cold north-westerly wind blows for a short period—often less than 24 hours. One of these winds is always followed by a crop of asthmatic attacks. During the summer there is a long period of relative drought, but the humidity remains very high. The dust and pollens from the bush which abounds everywhere undoubtedly play a part in the high incidence of hay fever during the dry period.

Comment on these factors and respiratory diseases has already been made by Dr. W. Santon Gilmour, in his able survey of tuberculosis in the Bahamas. Unfortunately this publication is probably not available to the general medical public. From time to time I have met professionally and in a private capacity individuals who have been sent here to a warm climate for the benefit of a respiratory condition such as asthma, chronic bronchitis, and bronchiectasis. Almost invariably these unfortunate persons have suffered a relapse sometimes of extreme severity. Bermuda, Jamaica, and other islands in this area appear to have as high an incidence of respiratory affections as we have here. It appears to me, therefore, that the attention of practitioners should be drawn to the fact that a warm, *humid* climate will probably do their patients more harm than good, no matter how beneficial a warm *dry* climate may be.—I am, etc.,

Nassau, Bahamas. W. H. P. POAD.

Sexual Disorders in Women

SIR,—Dr. Joan Malleson's article (December 22, 1951, p. 1480) would be timely even if only a fraction of her figures for frigidity and partial frigidity were true; though I think to some extent we are dealing with a cultural phenomenon, as well as individual maladjustment.

In psychiatric out-patient clinics I can only say that without special psychological presuppositions one comes across sexual difficulties so frequently that on the whole one only attempts to pursue those where their emergence is comparatively recent, the distress marked, and the patient of reasonable intelligence. This frequency is more understandable if one gives a large place in the total personality to the sexual drives; but in any case the adequate expression of them in the face of our culture remains more difficult for a woman than a man. There are, of course, also cases, such as depressions, where the lack of sexual feeling is only part of a general emotional disturbance. Those cases who have the insight and determination to complain frankly of their difficulties are more accessible, but not necessarily in less trouble, than those who complain of anything but their sexual difficulties. I have not always found that the hysterical anaesthesias are comparatively harmless, except perhaps on a short-term basis. In my cases, though, a picture of pure hysteria without some leakage of anxiety is not very common.

I think Dr. Malleson merits the fullest support in her attitude to clitoral orgasm. I have not found, though, that prudery is always the difficulty. The woman may feel, perhaps unnecessarily, that it all becomes a very planned affair, and as such underlines her inadequacy: she fears either losing sensation further, or reaching a high state of stimulation and then being unable to achieve orgasm. Much complicated emotional reaction may be implied in such an acceptance, and much here depends on the wife's feelings, not necessarily bad ones, to her husband, and his to her.

There is no doubt room for the various approaches of the gynaecologist, physician, surgeon, and psychotherapist, inspired, I hope, with humanity. These problems rarely stay individual for long, even if they were ever so in their general significance. Almost invariably a vicious circle of tension arises between wife and husband. Frequently one sexually maladjusted partner picks another, and what might be a minor difficulty becomes magnified out of all proportion. I feel, therefore, that an attitude of joint responsibility on the problem needs encouraging, and it is not only wise but accurate to avoid laying too much of the responsibility on one side.

The psychotherapy to be used needs definition. Some cases which are the result of deep maladaptation of personality are really only approachable by long-term analysis, and this is a very large undertaking. Others, especially the more superficial type, are treatable by the therapy of discussion, explanation, and support, admittedly often implying analytic interpretation, with or without physical and pharmaceutical aids—largely, I find, sedatives. In my experience the apparently most discouraging case does not always turn out to be so. In the shorter methods the patient cannot gain insight in the same way as by analysis, but in sexual matters the lack of voluntary control puts morale at a premium, and success with support may allow a patient to achieve more mature attitudes, which are also the long-term object of deep analysis. By this I do not imply any devaluation of analysis as a weapon of exploration, but only that for many patients a saving of money, but especially of time at such a crisis, may be crucial.—I am, etc.,

London, W.1. H. A. C. MASON.

SIR,—I think that Dr. Joan Malleson's article on this subject (December 22, 1951, p. 1480) is of considerable service, because this matter is not only imperfectly understood but very largely unrecognized, even in the profession of medicine, and there must be many practitioners who are not even aware of the separate existence of the clitoral and vaginal orgasm in woman. It is most certainly true to say that a large number of women never experience a vaginal orgasm at all, and if they are unaware—as many are—of its existence there is no worry attached to this fact; the worry comes from the absence of *any* kind of orgasm during intercourse, particularly if it can be brought about at other times by the process of masturbation.

I agree with Dr. Malleson that where there is a failure of orgasm in the presence of a repeatedly high-pitched erotic tension nervous symptoms will ensue, but in my experience these symptoms point to disturbances which cannot be explained without real knowledge of the woman, her life, and her personality. Anaesthesia is a satisfactory surface explanation, but it does not get us anywhere; its possible hysterical origin is a much more fruitful field, and is, in my experience, the root difficulty and supplies the reason why this anaesthesia is less amenable to therapy than are the other dysfunctions; it also provides the reason why those functional sexual disorders which are secondary to adult events are much more likely—indeed almost certain if handled rightly—to resolve.

If we assume that this anaesthesia is a hysterical conversion symptom and accept that its origin lies invariably in the repression of early infant sensations we are going to find it very difficult to deal with; if, on the other hand, we regard the conversion symptom as protective against an existing difficulty—that is, flight-reaction or negative response towards it—we shall succeed, provided that we can remove the circumstance or difficulty which has aroused the need for protection. But there is another factor which, in my experience, is of the utmost importance: it has been said—and I myself have no doubt of the truth of this—that in the true entity of hysteria there is an alteration in the ratio of the sex in the psyche. This would mean that the hysterical woman would possess a higher ratio of male to female in her personality, a state of things somewhat hostile to satisfactory sex relationship in so much as she will find it difficult to assume the passive role, *not* in the physical but in the emotional sphere. The markedly hysterical woman is, as I see her, utterly feminine to look upon but the very opposite as we search deeply into her. She can, and she often will, obtain a vaginal orgasm in sleep. She will wake with this to find the process continuing until it has exhausted itself in the usual way. If this should happen she will be disturbed, and she will search for the reason; she may even set out to test a new-found theory by an excursion into extra-marital relationship which, if it should succeed in producing this same orgasm, would be a disaster greater than the first, though for the time being she will have found a most satisfying "cure."

It is, of course, essential that a high pitch of erotic tension together with its accompanying tumescence should be relieved and especially so if it is often repeated, and I note Dr. Malleson's reference to the woman who, unable to obtain a vaginal orgasm, deprives herself of the relief of a clitoral one. She draws attention to possible thoughts of propriety and to the feeling that this is "all wrong" or "not natural," a view which I would say is as often, if not more often, shared by the husband. Dr. Malleson says that "a little sensible information on the matter can make a tremendous difference to some women." I would emphasize the word "some," for things do not always work out that way. A decongestion may well be brought about by the husband, but there are numerous cases in which only the woman can do this for herself; and these are the difficult cases, because it may well be that the husband is not the partner, as it were, in the emotional side of the union. Equally difficult, though in a different way, are those cases in which neither the husband nor the wife is able, by any means known to them, to bring about the much needed relief to congested pelvic organs.—I am, etc.,

Westham, Pevensey. MAURICE L. YOUNG.

SIR,—Dr. Joan Malleson's paper (December 22, 1951, p. 1480) must have been read with much interest and relief by practitioners whose medical education dates from pre-Freudian days. But even those who have accepted his teachings may not always derive from them the enlightenment and inspiration needed when dealing with those vexed cases of female orgasm inability. This is due to the fact that in these matters we are not without prejudice and that our conception of what constitutes a normal woman is still far too much influenced by memories of the times when, in matters of sex, woman was regarded as a kind of man in disguise. Very slowly only does the knowledge spread that a woman's sexual life history coincides nowhere with that of a man, that sexual reactions and manifestations normal to him may by no means be normal to her, and that we must investigate and judge her normality by purely female and not by male standards.

We might have wasted much less of our time and we might have avoided giving much misguided advice to our patients if, while investigating the orgasm riddle, we had not so deplorably lost sight of the biological aspect of the matter. A survey of the animal kingdom shows that in the majority of species, where the males are endowed with very efficient genital and extragenital organs of copulatory fixation, the active participation of the female is, teleologically speaking, unnecessary and in fact absent. In those

few species where neither genital nor extragenital organs of fixation have developed, the females do in fact participate, thereby facilitating fertilization. The present-day human race presumably finds itself midway between the anthropoid ape stage, where the female is solely an object of the male's sexual desire, and the human stage, where coitus takes place by mutual consent only. Always assuming that the object of sexual relations is fertilization and the survival of the race, neither the conditions prevailing on the sub-human nor those on the human plane seem to necessitate the development of female orgasmic ability, and it is not so surprising therefore that this trait presents itself as something that might be as well on its way in as on its way out (Terman).

For practical purposes meanwhile we must remember that in all women orgasmic ability is not, as in the male, a necessary, well-established sensation but a *noli me tangere*, capable of manifesting itself fully in ideal circumstances, partially on less auspicious occasions, and of remaining totally in abeyance if inhibited by one of the thousand causes so well known to psychologists. Only where we can remove all of them—and wherever we can we do that—may we expect a woman to display her full capacity. For the rest we must continue to remind her that the acme of her sex life and the source of the most intense and lasting pleasure are not to be looked for in coital activity but in the birth of her baby.—I am, etc.,

Pinner, Middlesex. EDWARD ELKAN.

Male Infertility

SIR,—I wish to draw attention to your leading article on this subject (December 22, 1951, p. 1507) and especially to the passage, "Some clinics find it difficult to persuade the husband to attend for interview or even to provide a seminal specimen."

I would remind you that the question of providing a seminal specimen is one of grave difficulty for Roman Catholics. The usual method of providing a seminal specimen is either by the use of a condom during sexual intercourse or by ejaculation into a condom or other vessel during masturbation or coitus interruptus. These methods are regarded by all Roman Catholics as perversions of nature and hence as intrinsically evil, and their use would be a grave sin. Since the question of sterility is a serious problem to many Catholic couples, I would urge that greater use be made of such methods of estimating male fertility as testicular biopsy and the excretion of gonadotrophins and androgens in the urine, which do not involve the committing of offences against the natural law.—I am, etc.,

Manchester, 12. F. N. VALDEZ.

Cerebral Blood Vessels and "Priscol"

SIR,—Recently (October 13, p. 891) Drs. S. Smith and E. C. Turton reported a case in which motor aphasia and agraphia were temporarily relieved by intravenous and oral "priscol." The authors attributed the therapeutic effects of the drug to its vasodilatory action in the affected area of the brain. In view of their statement that, "although many papers have emphasized the value of priscol in peripheral vascular states, none has been concerned with the effect of the drug on the cerebrovascular system," I wish to draw attention to some experiments of mine which confirm their clinical observation and their explanatory comment.

A window was made into the skull of adult cats under "nembutal" anaesthesia and pictures were taken through a capillary microscope before and after intravenous injection of 5 mg. priscol (technique to be described in detail elsewhere). In all ten experiments a prompt dilatation of the pial arteries and arterioles was observed, lasting up to seven minutes. The duration of the vasodilatation was not followed longer, the animals being used for another experiment. The veins were not noticeably dilated. Priscol had a vasodilatory effect also in cases in which vasospasm was produced by concussion. The effect is shown in the Figures. Fig. 1 was taken before, and Fig. 2 seven minutes after, intravenous injection of 5 mg. priscol. The results of these experiments, performed in 1941, were mentioned in a recent article (Engel, *Acta psychiat., Kbh.*, 1950, **25**, 153): "A drug which, as far as I know, has not been tried out in cerebral vascular affections of spastic nature is priscol. . . . I tested its effect on cerebral blood vessels by capillary microscopy through a window in the skull of cats, and found it to be a powerful vasodilator. . . ."

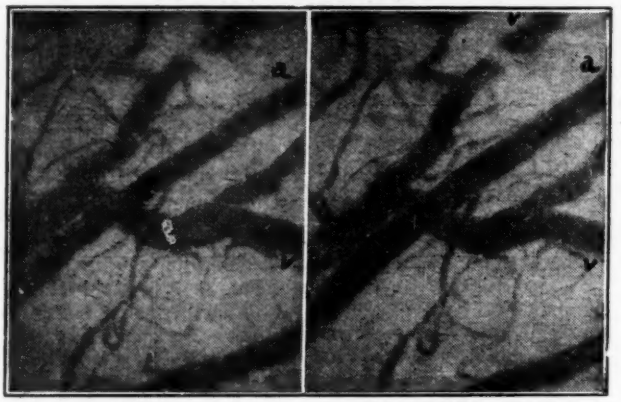


FIG. 1. FIG. 2.

"a" represents an artery, "v" a vein.

I am convinced, judging from Smith and Turton's report and my experiments, that in suitable cases priscol may have a salutary effect on the cerebral blood circulation. A trial should be given to it in cases of post-concussional syndrome, 5–6 weeks after trauma, in migraine, and in any vasospastic conditions in which no danger of cerebral haemorrhage exists. It may also be indicated in primary shock. The reduced blood pressure following injection might be an advantage.—I am, etc.,

Hong Kong. D. ENGEL.

L-*Nor*adrenaline as a Vasoconstrictor

SIR,—Some remarks on the blood pressure effects of D-methyl amphetamine ("methedrine") in Dr. H. C. Churchill-Davidson's most interesting paper (December 29, 1951, p. 1551) must be called in question. He states that L-*nor*adrenaline produces an almost similar rise of systolic and diastolic pressures, while methedrine produces only a slight rise of diastolic pressure in comparison with the systolic elevation. My experience with methedrine for correcting the hypotension accompanying high spinal blockade is not in accordance with this assertion.

In 300 cases under controlled hypotension intravenous methedrine has produced a diastolic rise of the order of slightly more than half the systolic rise. This is comparable with the systolic/diastolic pressor ratio obtained with *nor*adrenaline in Dr. Churchill-Davidson's data. I have measured the pressure rises shown in his charts in response to ten separate administrations of *nor*adrenaline, and compared them with the responses obtained from methedrine in a random sample of ten cases rendered hypotensive by high epidural block. The results are shown in mm. Hg:

Response to Noradrenaline. (Dr. H. C. Churchill-Davidson)

Data	Fig. 2	Fig. 3	Fig. 4
Systolic rise	25 53	68 300	74 65 65 71 90 38
Diastolic ,,	18 30	30 155	75 30 40 20 58 35
State	Haemorrhagic hypotension		Ganglion-blockade hypotension

Response to L-*Methyl Amphetamine (Methedrine)*

Dose of methedrine in mg.	5	5	6	6	5	6	6	7	4	6
Systolic rise	40	50	35	45	55	35	35	65	35	35
Diastolic ,,	35	35	20	25	45	30	20	30	25	20
State	Spinal block vascular hypotension									

It can be seen that in the figures from Dr. Churchill-Davidson's charts the diastolic rise averages 55.7% of the systolic rise in

response to *nor*adrenaline, while my figures for methedrine show an even greater diastolic response, averaging 61.1% of the systolic rise. Assuming that both our samples are fair ones, it must be concluded that under the clinical conditions obtaining methedrine produces a greater, and not a smaller, diastolic response than *nor*adrenaline.

This may seem to labour a comparatively trivial point, but there is much that we do not know about the response of the body to pressor amines under normal and abnormal conditions, and it is therefore all the more important to keep clear what data we have, as a sound foundation for our theory and practice.—I am, etc.,

Emsworth. P. R. BROMAGE.

Migraine

SIR,—The investigation conducted by Drs. D. A. Campbell, K. M. Hay, and E. M. Tonks (December 15, p. 1424) is of singular interest to all who have any interest in the aetiology of migraine.

The facts which have been elicited would, however, have been even more useful had the type of migraine from which each patient was suffering been made known. It is obvious to all who have any real experience of these periodic headaches, be it from an aetiological or a therapeutic standpoint, that there are various types of the disease. Some migrainous patients undoubtedly have a basic endocrine abnormality; others appear to suffer from only a form of allergic disturbance. For instance, it is difficult to imagine any glandular dysfunction which, of itself, would produce an attack of migraine twice a week; while it is equally true that a generalized desensitization with either prostigmine or, better still, histamine will, in a significant number of cases, bring about alleviation, if not cure. This occurs even though the attacks are not of the typical histamine headache type.

My own interest in migraine started when an attack was induced with an injection of oestradiol (*Lancet*, 1942, **1**, 488). A similar result has been noted, though not considered worth reporting, on several occasions since. A better means of permanently relieving such type of migraine is by means of anterior pituitary lobe hormone rather than progesterone.

Yet, though water retention is perhaps the cause of headache in a number of cases, there is equally no doubt that at least 50% of patients do not note any diuresis either before, during, or after an attack. This is a question invariably put by me to all individuals examined for migraine, whose number now totals almost 800.

While migraine is a disease about which we know relatively little, there is no doubt that proper treatment will bring about great alleviation if not complete relief in about 80% of patients, whose number increases daily. There is equally no doubt that the disease must be looked upon from a broad standpoint and no one single therapy is ever likely to be the answer to the relief of so complicated a syndrome.—I am, etc.,

Putney. NEVIL LEYTON.

Shortage of X-ray Films

SIR,—It has been common knowledge for some time that there is a serious shortage of *x*-ray films in this country, owing to two facts—40% export of British-manufactured *x*-ray films and an increased use of *x*-ray examinations as the result of the National Health Service.

In a recent circular letter headed "Economy in the Use of *X*-ray Film" (*British Medical Journal, Supplement*, December 8, p. 255), signed by the chief medical officer of the Ministry of Health, he states the increased use of *x*-ray films as 76% greater than in 1947 and advocates further reduction in the use of *x*-ray examinations. This of course is most unlikely, and instead of reduction there is likely to be a further increase.

Surely the real answer is for a long-term policy to step up production of films by increasing the factories producing these articles but as a short-term policy to reduce or entirely abolish the 40% quota of British-produced films being sent abroad to countries such as Egypt, etc., and so permit the British public to get the maximum benefit from their Health Service.

On the Continent there appears to be no shortage of films, and recently I brought back from France a small supply. I was charged 24% duty by the Customs, and they suggested a fine of 10s. because B.E.A. officials had loaded the films in the wrong end of the aeroplane, making them arrive as luggage instead of cargo. The fine was not paid, but surely if we are to be deprived of films let us bring them back to this country without this extortionate duty and ridiculous suggestion of a fine.—I am, etc.,

London, W.1. NORMAN P. HENDERSON.

Educating the Public About Cancer

SIR,—Dr. J. F. Brailsford's letter (November 10, 1951, p. 1154) should not be allowed to pass without comment, as it represents an attitude of defeatism towards cancer which is all too prevalent in the British Isles. It would be very difficult for Dr. Brailsford or anyone else to show that early diagnosis and treatment do not greatly improve the chances of five-year survival in a vast majority of cancers. With our present methods of treatment no one can deny that sometimes even the earliest apparent case is sometimes uncontrolled, but the chances of "cure" in the early case are very much higher than in the late case.

For the past 15 years or so there has been, in the United States and Canada, an intensive publicity campaign which has been carried out by voluntary organizations—the American Cancer Society and the Canadian Cancer Society. The result has been a very much more intelligent public appreciation of the early signs of cancer, and consequently a very much earlier diagnosis of the disease than obtains at the present time in Britain. In Saskatchewan, for instance, there has been an active Government-sponsored cancer control programme in effect since 1932 and the population has been exposed to intensive propaganda from the Canadian Cancer Society for more than 10 years. These two factors have resulted in a marked increase in the percentage of early cases of cancer seen in the Government cancer clinics in Saskatchewan (*Canad. J. publ. Hlth*, 1951, **42**, 427, and *Lancet*, 1951, **2**, 496).

From the years 1932 to 1944 (inclusive), 6,816 new unselected cases of cancer were admitted to the cancer clinics in this province. The crude five-year survival rate was 43% and the corrected five-year survival rate was 49%. Dr. Brailsford states he has known patients with untreated cancer live more than five years. It is undoubtedly true that occasional patients suffering from cancer do survive without treatment for this length of time. Has Dr. Brailsford, however, any statistical evidence to show that 43% of untreated cases of cancer live five years? He states that women have a nerve supply even in the breast, and cancer manifests itself to their notice before the doctor can feel it. A monograph on this very important new sign of his would be instructive to those of us who are daily confronted with women who have undiagnosed breast tumours.

Public propaganda on cancer to-day is aimed at the prevention of fear of the disease, and the incidence of so-called cancer phobia is very much lower than Dr. Brailsford seems to think. In any case, cancer phobia in itself has never proved a fatal disease. Having had some experience in cancer work, both in England and Canada, we can definitely state that there is far more fear of the disease and ignorance of its nature in England than in Canada. Man fears the unknown. What knowledge we have at present of the disease should be shared with the public, and the inevitable result will be a great increase in the number of early cases seen in tumour clinics. Dr. Brailsford's theoretical objections to public education in cancer just do not exist in practice.—We are, etc.,

Cancer Clinic, Saskatoon, Canada. T. A. WATSON. O. D. BERESFORD.

Death on the Roads

SIR,—May I endorse Dr. C. W. A. Searle's remarks (December 29, 1951, p. 1583) on the laxity of both the law and the public in their attention to the necessity for good vision in driving? I frequently see myopes who either have no glasses or, if they have, do not wear them for driving. After dark, these people are particularly dangerous. I was told once by one of the latter that as he could see a number plate at 25 yards with his glasses on he felt no difficulty about signing the licence declaration though he never wore his glasses. I was once travelling in a Service vehicle which overturned because the driver's eyesight was only 6/60 when I tested her eyes a day or two later. I have also seen a patient with diplopia who was still driving.

Very often when one is driving one can tell by the attitude of a pedestrian or by his gestures that he is probably going to do something foolish. To observe these hints demands a good standard of visual acuity and saves accidents. Many pedestrians are infirm and suffer from bad eyesight themselves. If one of these unfortunates coincides in his travels with a careless myope the danger is apparent. One can hardly prohibit pedestrians with poor eyesight from crossing the roads.

It might even be advisable to treat culprits as those suspected of being drunk, so that an eyesight test is included in the routine investigation of a motorist who has been involved in a serious accident; particularly the question whether he was wearing his glasses at the time should be raised. I feel sure that a more stringent application of the law would save lives.—I am, etc.,

Greenwich, S.E.10. P. A. GARDINER.

Trichlorethylene Analgesia in Labour

SIR,—In the article by Mr. O'Donel Browne and others (December 29, 1951, p. 1556) it is stated that it was difficult to provide analgesia for the normal delivery at home because Minnitt's apparatus was too heavy if there was poor transport; and that the use of narcotics required greater skill, experience, and supervision than they could supply.

Surely proper transport is essential for this work to be done well; and should not the skill, experience, and supervision necessary for the administration of the drugs also be considered the right of patients in their own homes? Perhaps the co-operation of general practitioners, who are accustomed to coping with the difficulties mentioned, could be enlisted. It is rather distressing to think that students and pupil midwives may be led to imagine that proper analgesia and any necessary drugs cannot be easily obtained in domiciliary practice.—I am, etc.,

Plymouth. O. LL. LANDER.

Haemolytic Disease of the Newborn

SIR,—I read with much interest Dr. W. Walker's fine review article on haemolytic disease of the newborn (November 10, 1951, p. 1142) in the *British Medical Journal*, and would like to make the following comments.

1. The statement, "Tests for the strength of antibodies are not of much value in predicting the form or severity of the disease in the baby, and are not required," is not correct. In our own experience with tests on about 600 Rh-negative women there was a definite correlation between the maternal antibody titre and the severity of the baby's illness. In 338 Rh-negative mothers who were not sensitized the total mortality rate (stillbirths and neonatal deaths) among the babies was only 1.5%, so that non-sensitized Rh-negative mothers have as good a chance of having normal babies as Rh-positive mothers. On the other hand, among Rh-positive babies from sensitized Rh-negative women the total mortality rate was considerably higher, and was correlated with the maternal antibody titre. Thus, when the antibody titre was four units or less by the albumin-plasma conglutination method the total mortality rate was 12.2%, while with titres ranging from 65 to 256 units the total mortality rate was as high as 72.2%. With Rh-negative babies the height of the maternal Rh antibody titre was inconsequential, because none of those babies were erythroblastotic.

2. The assertion that one can predict the Rh type of the unborn baby from the Rh types of the parents requires some qualification. For example, if the husband belongs to type Rh_1Rh_1 his genotype could be either R^1R^1 or R^1r', of which the former is by far the more common and therefore the more likely. In general, therefore, one may assert with reasonable certainty that such a husband is homozygous for the Rh_0 factor, and that every child will be Rh_0 positive, and if the mother is sensitized that the expected baby will therefore be erythroblastotic. One must bear in mind, however, the possibility of rare instances where the husband is actually of genotype R^1r', in which case there is a 50% chance that the baby will belong to type rh' and therefore will not be harmed by the maternal Rh_0 antibodies. A similar qualification must be made when the husband belongs to type Rh_2Rh_2, in which case his genotype could be R^2r'' as well as R^2R^2. Finally, individuals of type Rh_1Rh_2 are not always homozygous for the Rh_0 factor, because they could belong to genotype R^1r'' or $r'R^2$ as well as R^1R^2, to say nothing of the rarer genotypes involving genes R^z and r^y.

On the other hand, individuals of phenotypes Rh_1rh and Rh_2rh are not necessarily heterozygous. For example, a person of type Rh_1rh might belong to any of the three genotypes R^1r, R^1R^0, or R^0r', of which the first is the most common and therefore the most likely. While most individuals of phenotype Rh_1rh are heterozygous, if a type Rh_1rh husband of a type rh woman has had two children, one type Rh_1 and the other type Rh_0, his genotype would have to be R^1R^0, so that such a man would be homozygous for the Rh_0 factor.

Where the husband is definitely heterozygous, as proved by the previous birth of an Rh-negative baby, there is a 50-50 chance that any future baby will be either Rh positive or Rh negative. By watching the course of the antibody titre during pregnancies one may be able to predict the Rh type of such a baby. If there is a significant rise in antibody titre at any time during the pregnancy, the foetus must be Rh positive. In not one of 16 cases studied by us in which the foetus was Rh negative was there a rise in antibody titre at any time during the pregnancy or after delivery, so that reports of so-called non-specific anamnestic reactions are based on faulty technique of titration. Failure of the antibody titre to rise leaves open the question whether the baby is Rh positive or Rh negative. However, in such cases where the antibody titre had been at a high level (250 units or more) throughout the pregnancy, we have predicted correctly shortly before the birth of the baby that it would prove to be Rh negative, reasoning that were it Rh positive it should have died *in utero* by the seventh or eighth month.—I am, etc.,

Brooklyn 25, N.Y. A. S. WIENER.

SIR,—I appreciate Dr. A. S. Wiener's interest in my article on haemolytic disease of the newborn and feel that his remarks require comment. I would remind him that the article was written for the guidance of the family doctor. Detailed consideration of the more controversial issues was therefore outside its scope. I will consider his two points in turn:

1. Throughout the past 10 years many attempts have been made to relate the antenatal maternal antibody titre to the subsequent form and severity of the disease in the infant. The results have been equivocal. In my hands, tests for the strength of maternal antibody using titrations in saline, albumin, and by the indirect Coombs test have been of little value in the individual case. I have found only a vague correlation between antibody strength and prognosis, though it may have some value in the prediction of still-

birth. This is not sufficient to influence one's conduct of the individual case, especially when one considers the multiplicity of tests required.

2. Dr. Wiener would, I think, agree that the knowledge of the father's genotype is of value (due consideration being given to the specificity of the antibody concerned). In his letter he is apparently solely concerned with the difficulty of determining this by serological tests on the father's blood. When preparing my article I decided that a discussion of these points was inappropriate. Dr. Wiener's letter leaves me unrepentant.—I am, etc.,

Newcastle-upon-Tyne. W. WALKER.

Childhood Factors in Duodenal Ulcer

SIR,—Dr. A. Balfour Sclare's letter (December 8, p. 1405) discloses one of the fallacious premises in Dr. Kellock's study (November 10, p. 1117). The other is that Dr. Kellock used as a control group people who were ill enough to be under the care of a hospital. The assumption is that none of them were suffering from diseases caused by emotional difficulties. Why should this assumption be made? Until a comparison has been made between people ill in hospital and people of similar age, occupation, etc., who have never been seriously ill, it is not proved that emotional conflict is not the prime cause of *all* disease. In such a comparison the factors influencing personality should, as Dr. Sclare points out, include those currently regarded by psychological authorities as being most important in producing emotional conflict in some individuals. Clearly such a piece of work would entail the spending of much time and patience, but the results might give the protagonists of "psychosomatic" medicine some very sure ground to stand on.—I am, etc.,

London, E.1. ALAN WATSON.

Gastric Carcinoma and Acute Perforation

SIR,—The risk of malignancy in perforated gastric ulcer has, of course, been known for some time. Of a personal series of 44 perforations six were gastric in type. In view of the known risk, once again stressed by Mr. Terence L. Kennedy (December 22, 1951, p. 1489), wherever possible excision of the ulcer was carried out and repair of the stomach performed. This had two advantages: the induration and oedema sometimes found may make suturing difficult and closure uncertain—the clean-cut edges of the operation excision can be sewn together with ease, making repair simple. Complications such as fistula formation, which occasionally occur, are thus avoided. The second advantage is that the whole ulcer area can be sent for section and the diagnosis of malignancy made with certainty and speed. There has been no difficulty when this procedure has been carried out. In Mr. Kennedy's series this manœuvre was not possible in all cases, since a number of these had obvious tumours, but it should be kept in mind and employed more often.

Finally, gastric carcinoma may occur with an independent gastric ulcer and a case of simultaneous perforation must be unusual. Without going into clinical details, which were not exceptional and presented a typical picture—a carcinoma of the pylorus was found to be perforated, and on the body of the stomach, quite separate, was a clear-cut independent ulcer which had also perforated.—I am, etc.,

Stourbridge. MAURICE HERSHMAN.

"Robaden" and Enterogastrone

SIR,—The note on "New Treatments of Peptic Ulcer" contained in "Any Questions?" (October 6, 1951, p. 862) has come to my attention. The attitude of caution taken by the commentator is most commendable, but certain misstatements require correction. The Swiss preparation "robaden" is compared with the enterogastrone preparations of the American workers as though both were only different brand names of a common preparation. Actually what has come to be known as "enterogastrone" is an extract of the mucosa of the upper small intestine: it would appear to be of a protein nature: its chief pharmacological action is inhibition of gastric secretion. Robaden, on the other hand, is a protein-free extract of the total stomach and small intestine and does not have the pharmacological action of enterogastrone in depressing gastric secretion. Without exception the papers published in America have dealt with enterogastrone only, and it is therefore obvious that conclusions drawn from the American studies cannot be applied to robaden.

Among the European papers you cite you have stressed one which gives attention to the importance of psychological influence of the doctor on the ulcer patient. Although psychological factors in the therapy of ulcer disease play an important part—as they do also in other chronic diseases such as arterial hypertension, rheumatic processes, etc.—sustained success in therapy cannot be achieved by the administration of placebo preparations.

May I draw your attention to the fact that in 1944 I was the first to report on good results with robaden in ulcer therapy? In 1951 I published a second paper on our findings since 1944, and could report confirmation of the earlier good results obtained by me and my colleagues.—I am, etc.,

Solothurn, Switzerland. H. SCHMASSMANN.

Technique of Shock Therapy

SIR,—It is my experience that both "tubarine" and "flaxedil" can produce a sense of suffocation in the conscious patient even when administered in smaller doses than those mentioned by Dr. D. T. Maclay (December 15, 1951, p. 1464) and that it is the apprehensive or uncooperative patient who is most likely to show distress. Dr. Maclay finds his technique to be satisfactory for a special type of case, but in principle it seems undesirable to allow these drugs to develop their effects without the cover of some form of narcosis. I believe that there are very few patients to whom a sleep dose of thiopentone may not be administered with safety, provided that they are given oxygen to breathe—preferably beforehand—and are kept well oxygenated up to a moment of stress.—I am, etc.,

Huyton, near Liverpool. J. R. ESPLEN.

Antihistaminics in Rheumatoid Arthritis

SIR,—I was interested to read in Professor Edward C. Kendall's Heberden Oration (December 1, 1951, p. 1295) that he seems to favour the view that rheumatoid arthritis may be due to a hypersensitivity state. If the disease were the result of the combination of an antigen (i.e., a foreign protein) and an antibody, cortisone could act either by modifying the rate of production of the antigen or by protecting the tissue from the effects of the products of such a combination. Presumably histamine, or a histamine-like substance, is likely to be involved.

So far as I know antihistamine drugs have no effect on cases of established rheumatoid arthritis, but the following case may be of interest in this connexion.

A middle-aged woman had been subject to fleeting attacks of pain and swelling in various joints for just over a year. The attacks came on suddenly and affected chiefly wrists, elbows, knees, and ankles. The pain and swelling generally subsided in a day or two, and there was no residual disability.

The attacks had been becoming more frequent and severe in the two months prior to her attendance at the clinic, and she was developing minimal swelling with stiffness of the proximal interphalangeal joints of the fingers. I diagnosed "palindromic rheumatism," which, in my experience, is generally an unusually prolonged period of prodromal symptoms heralding the onset of true rheumatoid arthritis.

However, in view of the fact that some authorities regard palindromic rheumatism as a separate entity due to an allergic state, I suggested to the patient's doctor that it might be worth while trying the effect of "anthisan" (one tablet thrice daily). This drug produced a dramatic relief of symptoms. The patient has not had any pain or swelling in any joints for over three months, and the swelling in the interphalangeal joints has subsided.

I have tried the effect of this drug on several similar cases in the past and it produced some symptomatic relief in all. I am aware that these observations are not in any way conclusive, but it would be of great interest to learn what success other practitioners have had in treating rheumatic diseases with antihistamine drugs.

In view of the absence of any direct proof that rheumatoid arthritis can be attributed to a hypersensitivity state any indirect evidence to support such a theory is of special importance.—I am, etc.,

Watford. RICHARD W. BARTER.

POINTS FROM LETTERS

"Primary Atypical Pneumonia"

Major D. HAMILTON (B.A.O.R. 16) writes: A lot of "atypical pneumonia" I have seen bore little resemblance to the disease described by Dr. D. M. Baker (November 24, p. 1277). It was very easily diagnosed. It must be remembered that Coxsackie viruses, *Rickettsia burneti*, and the influenza viruses are all occasionally indisputable causes of the typical pneumopitis. The most promising approach to the subject is through the laboratory. The picture of benign pneumonitis varies greatly with place and time both in course and cause. As I saw it in Cyrenaica it was probably aspiration pneumonia, for it strongly favoured the dependent segments and subsegments, especially the axillary subsegments and the apical segment of the lower lobe. As originally described by a U.S.A.M.C. major it was thought to be influenzal. . . . We are shaking the mantle of the Oslerian tradition off. Just as well. The reconciliation of the divorced parties of diagnosis and treatment under the one approach of management of the case, and the recall of treatment from the wilderness, was essential. The Oslerian tradition, with its overemphasis on passive observation rather than management, did not even result in a complete catalogue of the common diseases. This is not to criticize the efforts of these physicians. Their approach was necessary. It has served its purpose.

Registered Drug Samples

MENLEY & JAMES write: We have received reports of annoyance caused to doctors by the early delivery of registered packets containing samples (see *Journal*, November 24, 1951, p. 1285). A number of drugs and preparations which are controlled by the Poisons legislation may only be supplied against the *signed* order of a registered medical practitioner, and when supplied through the post they must be sent by registered post. We have followed this procedure for a number of years, but it seems that, paradoxically, because of improvement in the postal delivery services it is now giving rise to annoyance. We have taken up the matter of delivery with the Post Office, and in consultation with them we are arranging to incorporate on registered packages sent in response to requests for samples the following wording: "Postmaster—not first delivery, please." We can only make this request, but we understand that if a doctor complains to his local post office that he is being disturbed at an early hour by the arrival of packages the local office would arrange for packages to arrive during a later delivery.

Incontinence in a Woman

Dr. S. BRENNAN (Nottingham) writes: It is easy enough to enumerate the causes of incontinence in a man, but what of incontinence in a woman? Recently I received a 'phone message from a woman who appeared by her tone to be in great anxiety. When I arrived she told me that her urine was constantly dribbling. She gave me a history of this going on for a few weeks, but only after micturition, and she had paid little attention to it; but one day it became continuous—and thus her urgent 'phone call. I visualized a fibroid or a growth or some displacement. Abdominal examination revealed nothing. When I proceeded to do a P.V. I found complete atresia of the vulva, which was completely shut off by a thin membranous tissue. There was just a pin-point opening, surrounded by a red areola. Next day I examined her under an anaesthetic and broke down and stretched the membrane. She has been perfectly well ever since. She is a woman of 62 years, strong, healthy, and not of the neurotic or hysterical type. At the age of 31 she gave birth to a 9¼ lb. (4.1 kg.) baby, this being the only child. It was a normal delivery, but she was badly torn and required several stitches. Here was the extraordinary case of a woman urinating into the vagina and thence through this tiny opening, giving rise to the incontinence. I should like to know if this is an unprecedented case. I have never seen anything like it in my 30 years of practice.

Obituary

Dr. G. L. THORNTON, who died on December 4, 1951, at the age of 79, will be remembered with affection by a wide circle of ex-Service men and women, members of the Regular Armed Forces and the Territorial Army whose services extend over the two world wars. George Lestock Thornton was educated at Rossall School, Trinity College, Cambridge, and St. George's Hospital. He qualified in 1897, and after a period of general practice at Holt, Norfolk, and Ilfracombe, North Devon, he returned to St. George's Hospital as casualty officer and medical registrar before setting up again in general practice in Exmouth, South Devon, in 1903, in which year he obtained the M.R.C.P. He was a keen and shrewd clinician who strove always to keep abreast of expanding medical knowledge, and at the same time never losing the human and kindly touch of the family doctor. For many years he was secretary of the Devon and Exeter Medico-Chirurgical Society and medical officer to the Exmouth Cottage Hospital. In addition to the duties of a busy professional life he did not shirk civic responsibility and served on his local district council (whose chairman he was at the outbreak of the first world war, and again in 1919) and later on the Devon County Council. In 1915 he volunteered for service with the Royal Army Medical Corps and served first in Malta and later in France, Salonika, and Palestine with the 2/6 London Field Ambulance. He was awarded the M.C. and bar while acting as regimental medical officer to the 303 Brigade, R.F.A. After returning to general practice in 1919 for a short period he accepted full-time employment with the Ministry of Pensions Medical Services, becoming Deputy Commissioner of Medical Services, Exeter, which post he held until his retirement under the age limit in 1937. In recognition of his service he was appointed C.B.E. At the outbreak of the second world war he was recalled to temporary duty and served as Commissioner of Medical Services, South-west Region, until the conclusion of hostilities. Between the two wars he devoted much time to the Territorial Army, commanding the 128 Wessex Field Ambulance and later becoming A.D.M.S. of 43 (Wessex) Division and honorary colonel, 43 Division Medical Services. He held the post of Honorary Physician to King George V from 1930 to 1934. Always keenly interested in the welfare of ex-Service men and women, he was a member of the British Legion and took office as president of his local branch on his final retirement from the Ministry of Pensions. He married Letitia Anna Cordner in 1898. During the second world war he suffered the tragic loss of his wife, who was killed in a daylight air-raid on Exmouth in 1943, when his house was totally destroyed. He is survived by his three sons, two of whom are members of the medical profession, and one daughter.

Dr. NESTOR JOHN STANLEY NATHAN died on December 13 after a short illness at the early age of 41. He was a student at Charing Cross Hospital and qualified in 1932. After appointments as house-physician and house-surgeon at his own hospital, and as house-physician at the London Chest Hospital, he began his career in public health as an assistant medical officer at the Surrey County Council's Sanatorium at Milford. He then moved to the West Riding of Yorkshire, where he remained 13 years, first as assistant county medical officer of health and subsequently as medical superintendent first of the General Hospital at Wakefield and then of the Staincliffe Hospital, Dewsbury. It is particularly as holder of these two last appointments that he will be remembered in the West Riding with gratitude and affection, since it was due in no small measure to his enthusiasm and inspiration that these two hospitals were entirely transformed from backward institutions into the modern and fully equipped general hospitals they are to-day. In 1943 Dr. Nathan took the D.P.H. and in 1946 the D.R.C.O.G. In 1950 he returned

to public health as area medical officer for the Staffordshire County Council, but unfortunately his untimely death has cut short the excellent work he was doing in that sphere. He leaves a widow and two young sons, to whom the sympathy of his friends and colleagues will be extended.

Dr. ANDREW BROWNLIE died on December 13, 1951, at his home in Hamilton at the age of 75. He graduated M.B., Ch.B. at Glasgow University in 1899, and after two years' service as an assistant medical officer in Brislington Hospital, near Bristol, he became assistant in 1902, and partner in 1904, of the late Dr. James Adam, of Hamilton. When Dr. Adam gave up general practice to specialize in throat and nose work, Dr. Brownlie carried on the practice on his own until January, 1951, when ill-health caused his retirement. He had celebrated his jubilee in medicine 18 months before. During the first world war he served for two years in the R.A.M.C., mainly in Egypt and Malta. A regular churchgoer, he was an elder for many years. Though of quiet and reserved disposition, he was popular with his colleagues and patients. In 1932 he served for a year as chairman of the Lanarkshire Division of the B.M.A. He was a keen bowls player, and won prizes over many years. His wife predeceased him in 1942.

Dr. WILLIAM HOLBERTON SQUARE died at his home in Leighton Buzzard on December 18 at the age of 91. He had been in practice in the town since 1898. A member of a well-known Devon family, he was born at Kingsbridge, South Devon, and educated at Sherborne School and St. Bartholomew's Hospital. When he was a student he dissected with D'Arcy Power, and he delighted to tell stories of Matthews Duncan and Tom Smith. After qualification in 1884 he went into practice at Newton-le-Willows, in Suffolk, and from there he went to Sunderland, where his busy general practice included over 150 "midder" cases a year. Anxiety about his wife's health caused a move south, and he came with three young children to Leighton Buzzard just before the end of the century. Life was leisurely. There were no regular surgeries, and hunting with the stag-hounds in winter provided relaxation. Visiting in those days was done on horseback by day and a bicycle at night. Then a smart American "buggy" provided more comfortable transport, and in 1907 a baby Peugeot was obtained, succeeded from time to time by more roomy and reliable cars. Hunting continued to be his favourite relaxation until at 73 he had a fall and injured his shoulder. Even after that a horse was favoured for a few afternoon visits after the bulk of the work had been done by car in the morning. He was medical officer of health to the Eaton Bray Rural District Council until it merged into Luton Rural District Council, and to the Wing Rural District Council for 27 years, until after his 90th birthday. He was an active Freemason and was made a Grand Deacon of England in 1937. To successive generations in his practice he became an institution. He had never been ill—three days at the outside with mild influenza was all he could remember—and to many of his patients it seemed impossible that a time would come when he could no longer pay his usual visits. But 10 days before his death he felt too tired to carry on, and the end came just three weeks after his 91st birthday.—A. O. B.

Dr. WILLIAM ALFRED CARDEN died suddenly on December 27, 1951, in Johannesburg at the age of 79 years. He studied medicine at Guy's Hospital, qualifying in 1895. Four years later he went to Korea, where he worked as a medical missionary with the English Church Mission. In 1903 he settled in South Africa and began to practise at Fraserburg. Some years later he moved to Bothaville, in the Orange Free State, where he was in practice for 22 years: for a time he was district surgeon there. In 1930 he moved again, this time to Worcester, in Cape Province, and he continued in practice there until his retirement in 1942. He then settled at Deneysville, where he lived until the time of his death. His passing will be mourned by many of his colleagues in South Africa.

Medico-Legal

RESTRICTIVE COVENANT APPEAL DISMISSED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On December 13, 1951,[1] the Court of Appeal dismissed the appeal of a doctor against the decision of Mr. Justice Danckwerts, previously reported in these columns,[2] upholding a restrictive covenant in the partnership deed of the partnership from which the doctor had recently retired and granting an injunction forbidding him to practise as a general medical practitioner within a radius of 10 miles from Atherstone Parish Church.

In his judgment the Master of the Rolls said that, although the evidence showed that only 1% of the patients of the practice lived outside a radius of five miles, that 1% included the more affluent private patients who had cars to take them to the principal surgery, and accounted for more than a third of the total income. He found nothing vicious in the 21-year time restriction in the covenant, because, although this might amount to life banishment from the area, a doctor was a relatively mobile person and the whole of the United Kingdom was open to him. Nor did he find anything unreasonably wide in the covenant's formula "directly or indirectly carrying on or being interested or concerned in carrying on the business or profession . . ." Such a formula used in connexion with professional men did not carry the covenant beyond what was reasonably required to protect the continuing and remaining partners against competition. Accordingly, if radius, length of time, and the width of language used were taken, the total result of the covenant did not produce anything unreasonably wide.

His Lordship then went on to consider the effect on the matter of the National Health Service Act, 1946, and the Amending Act of 1949. While the plain intention and effect of Section 35 of the 1946 Act was to prevent doctors who practised, as these doctors did, in the Service from selling the goodwill of their practices, the section did not have the effect either of destroying the goodwill or of vesting it in the State or any emanation of the State. Goodwill remained one of the assets of the firm, on the creation and preservation of which the livelihood of the partners continued substantially to depend. This view of the matter was implicit in Section 1 (5) and (12) of the Amending Act of 1949, which showed that the element of goodwill was not so taken away that the ordinary principles otherwise applying to this restrictive covenant no longer did so. Nothing in the new legislation therefore invalidated this covenant, which was a valid covenant when made in 1945.

Lord Justice Birkett and Mr. Justice Upjohn concurred in dismissing the appeal and affirming the order of Mr. Justice Danckwerts, and the enforcement of the injunction was suspended until December 31, 1951.

[1] *The Times*, December 14, 1951.
[2] *British Medical Journal*, November 17, 1951, p. 1225.

Universities and Colleges

UNIVERSITY OF OXFORD

G. W. Corner, Hon. D.Sc., Director of the Department of Embryology of the Carnegie Institution, Johns Hopkins Medical School, Baltimore, U.S.A., has been appointed George Eastman Visiting Professor for the academic year 1952–3.

UNIVERSITY OF CAMBRIDGE

The following candidates have been approved at the examinations indicated:

FINAL M.B. (Old Regulations).—*Part I: (Surgery, Midwifery, and Gynaecology):* D. M. E. Allan, R. E. C. Altounyan, J. D. C. Anderson, P. A. J. Ball, B. W. Broadhurst, D. Bryant, H. M. Buckland, N. V. D. Bunker, A. R. Butterfield, H. Caplan, W. J. Colbeck, C. E. T. Cones, H. C. Cunningham, J. G. Davies,

J. I. W. Davies, R. J. L. Davis, R. H. Davison, P. J. Dawson, J. R. Edwards, J. N. T. Evans, J. R. Flury, J. M. A. Jepps, J. H. Jones, D. H. Kay, J. Liddell, A. B. Lowther, P. J. Lyne, P. J. McQuade, G. C. Metcalfe, H. Nichol, P. S. Reay-Young, W. A. G. Roper, T. L. Scully, M. P. Siddons, E. P. Simkin, J. D. H. Slater, D. M. Surrey Dane, M. L. Thomas, D. H. Trapnell, R. M. Turner, R. F. Warnock, O. H. Watkins, W. G. Williams, E. A. Wilson, D. Wise. New Regulations.—*Part II* [3]*Principles and Practice of Physic,* [3]*Surgery,* [4]*Midwifery and Gynaecology* (the figures indicate the section or sections passed): [4]J. F. Andrewes, [4]G. S. Banwell [2]A. J. F. Barratt, [3 4]A. W. Beard, [2]A. C. Beatty, [2]L. J. Bishop, [2]A. P. Blower, [4]C. J. Booth, [3 4]M. J. Boyle, [4]I. M. Brown, [2 3]G. M. B. Bulman, [2]D. M. J. Burns, [4]J. B. Chapman, [2]D. Churchill-Davidson, [2]M. J. Clarke-Williams, [2 3]R. G. Covell, [2 3 4]W. Eade, [2 3 4]J. C. B. Fenton, [2]R. V. Fiddian, [2]R. D. France, [2]H. W. S. Francis, [4]R. T. Gaukroger, [2 4]N. Gee, [3]H. M. Gough, [3]H. Gough-Thomas, [4]H. Graham, [2 3 4]G. P. Greenhalgh, [2 3]E. Hainsworth, [4]A. M. Harington, [3]D. Harrett, [3 4]R. J. H. Harris, [2]D. L. Harrison, [2]L. B. P. Hartley, [2]R. D. Hernaman-Johnson, [2 4]A. H. R. Hewett Clarke, [2]J. D. M. Howat, [3]R. L. Huckstep, [4]R. F. Ingle, [4]R. Keeley, [2 3 4]I. H. Kerr, [2]I. Lenox-Smith, [3 4]N. R. Lewis, [2 4]J. A. McHardy, [3 4]R. E. Mackie, [3 3]C. R. Maddock, [3]J. W. E. Mark, [2 3 4]K. J. Martin, [3 4]Mrs. C. M. Maxwell, [2 3 4]A. A. E. Nakeeb, [4]J. H. Newton, [4]T. F. D. Oram, [3]K. C. Paterson, [3]G. W. Pearson, [3]R. F. Pearson, [2 3]A. O. Peters, [2 3]R. A. N. Petrie, [3]J. M. Phillips, [2]C. Rashbass, [2]T. L. Ringrose, [2]V. Sarma, [4]C. W. Savile, [4]G. E. Sharp, [2]G. M. Shaw, [4]L. P. Sheil, [2]G. W. Smallcombe, [3]J. A. J. Smith, [4]J. L. Somervell, [2]E. M. Sproston, [2]R. M. Standish-White, [4]N. A. Subedar, [2]P. H. Swinhoe, [4]B. V. Tyman, [2 3 4]B. G. S. F. Vergano, [2 3 4]G. T. Whitaker, [2]R. E. Wolfendale. Old Regulations.—*Part II (Principles and Practice of Physic, Pathology, and Pharmacology):* G. B. Davison, D. A. Edington, P. S. Greaves, D. W. Hall, J. F. Higgins, A. Paneth, D. G. D. Vint. New Regulations.—*Part I (Pathology and Pharmacology):* C. W. M. Adams, P. G. Allen, M. A. Baddoo, A. W. Beard, D. W. K. Bird, L. J. Bishop, M. H. H. Bishop, Mrs. N. L. Blackwell, A. P. Blower, G. M. P. Boyes, J. E. Brett, H. G. Britton, D. M. J. Burns, D. A. P. Burton, T. F. Bushby, V. G. Caiger, C. McC. Campbell, D. Campbell, G. R. C. Campion, S. M. Cannicott, C. E. Channon, J. B. Chapman, W. H. Chapman, D. Churchill-Davidson, Mrs. G. Cole, R. R. A. Coles, A. S. Cooper, B. R. Corbin, M. J. F. Courtenay, R. G. Covell, S. H. Dallas, P. F. Dixon, A. B. Donnison, M. Dulake, J. H. Edwards, R. V. Fiddian, S. J. Fisher, Mrs. H. French, O. H. French, I. M. Glynn, R. Goldsmith, A. N. Griffith, H. F. Grundy, M. C. Guard, T. Hall, E. B. D. Hamilton, D. L. Harrison, R. Harrison, M. W. A. Haward, A. L. Hilton, J. A. Holland, B. L. Hoskyns, J. D. M. Howat, J. Innes, B. S. Jay, D. S. Jeffery, A. McL. Keil, I. H. Kerr, E. I. Kohorn, J. S. H. Lodge, R. Mangnall, K. J. Martin, R. J. Mather, G. G. Matthews, P. L. Maybury, N. A. Miles, K. F. Morrice, T. M. O. Morris, D. B. Murray, J. F. Newcombe, J. H. Newton, J. O. Ojukwu, D. N. H. Owen, W. N. B. Parker, K. C. Paterson, G. W. Pearson, A. O. Peters, J. M. Phillips, J. T. H. Pick, P. F. Plumley, J. F. Preece, P. M. H. Rack, G. L. S. Rankin, C. Rashbass, J. M. Rigg, T. L. Ringrose, R. W. Ross Russell, K. E. K. Rowson, J. H. Sewart, C. A. Sharples, H. J. Shimmin, J. M. Simister, F. V. Simpson, R. L. Smith, R. J. Spray, J. H. Swallow, K. A. Taylor, D. S. Trouton, J. A. M. Tudor-Hart, K. M. Underwood, G. I. Verney, M. F. R. Waters, J. Watson-Farrar, P. A. Watt, I. Weinbren, G. T. Whitaker, J. S. H. Whitehead.

UNIVERSITY OF ABERDEEN

At a Graduation Ceremony held on December 19, 1951, the following medical degrees were conferred:

M.D.—R. E. Glennie, P. O. Leggat, A. W. B. MacDonald.

M.B., CH.B.—[1]Q. A. F. R. Grant, [1]S. G. B. Innes, [1]L. Symon, [2]S. R. McN. McCreadie, [2]N. MacLeod, [2]G. M. Mitchell, Catherine K. Adam, R. G. G. Allan, J. A. Anderson, Mary I. R. Auld, L. B. Bartlet, A. G. Beattie, Anne C. Biezanek (née Greene), Emma L. Birse, R. F. Blackburn, R. Brown, K. S. Cameron, J. D. Campbell, G. W. Cardno, R. A. Christie, A. G. Craig, Shiela W. Craig, J. H. F. Crawford, R. Davidson, Madeline Deans (née Ross), J. I. D. Diack, I. M. Dingwall, R. T. Donald, Caroline S. Duff, Janet C. Duncan, J. M. Farrell, J. A. Forbes, Enid Fullerton, E. R. Fyfe, A. Gage, R. Gardiner, A. Gatherer, G. H. M. Gordon, A. J. Graham, Elizabeth D. Grassie, H. Gray, Elizabeth A. Green, Jean C. Hay, A. Herriot, R. D. Hill, H. M Horne, L. F. Howitt, C. G. Ingram, I. M. R. Laing, T. R. Lawrie, A. R. Lyall, A. Lyon, Betty McAllan, D. S. McDonald, M. E. McDonald, A. Macinnes, Mary MacIver, W. G. McKay, Mairi MacKenzie, A. R. McNaughton, D. MacNeill, Joyce M. Millar, D. Milne, June I. Milne, K. G. S. Milne, A. Minto, H. Nicol, Margaret H. Norquay, H. E. Nutten, S. Peace, B. G. Pirie, Sheila M. Purchase (née Dawson), Norah P. Raitt, H. P. Robb, R. C. Roll, Lilian M. Scotcher, R. McD. Scott, P. O. Sharp, E. J. Sinton, R. Stalker, A. K. Stephen, Edith G. Stewart, W. J. S. Still, J. S. Taylor, E. R. H. Tennant, J. B. Troup, A. G. Turner, C. H. Walker, J. M. R. Wetherly, R. E. Wetherly, Agnes E. Whitter, A. F. Whitter, R. V. Williams, G. A. Wood.

[1]With honours. [2]With commendation.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following medical degrees were conferred on December 6:

M.D.—T. T. Chapman, E. R. N. Cooke.

M.CH.—J. E. F. Coolican.

M.A.O.—A. D. H. Browne.

M.B., B.CH., B.A.O.—N. Boland, Norma E. Boyd, Iris E. Byers, E. D. Cooke, D. L. Cowan, Patricia G. Ellis, Phyllis E. Featherstone (formerly McCready), K. W. M. Harbord, W. Jackson, Ethel G. Jennings, T. D. Kimmet, R. King, G. J. Malseed, Edith P. Pringle, Aileen F. Smith, W. McC. Wilson, B. W. Withrington.

UNIVERSITY OF LONDON

The following candidates have been approved at the examinations indicated:

M.S.—*Branch I (Surgery):* A. G. Ellerker, B. W. Wells. *Branch IV (Otology, Rhinology, and Laryngology):* J. A. Harpman.

UNIVERSITY OF SHEFFIELD

At a Degree Congregation held on December 18, 1951, degrees in the Faculty of Medicine were conferred as follows:

M.D.—G. M. King.

M.B., CH.B.—A. H. Askew, Phyllis B. Banks, Hilda M. Brunt, D. A. Ewing, M. Falconer, G. Flowers, Phyllis B. Hobbs, J. K. Johnson, J. H. Nicholls, D. L. Price, Mrs. Zoe C. Randall, Olga R. Raphael, D. Waddington.

QUEEN'S UNIVERSITY, BELFAST

At a Graduation Ceremony held on December 19, 1951, the following medical degrees were conferred:

M.D.—[1]R. F. Whelan, [2]Wilmert F. I. Brown, [2]W. F. McAuley, W. Bingham, W. B. S. Crawford, J. K. A. Dorman, S. Kay, K. L. Stuart, A. P. Trimble, D. G. C. Whyte.

M.CH.—H. C. Dales.

M.B., B.CH., B.A.O.—Adela M. Blair, Sarah F. Charlton, D. McL. F. Drew, L. Fenton, J. L. Houston, T. J. McCabe, G. A. McCann, J. J. McCavana, I. A. McQuade, H. G. S. Murray.

[1]With high commendation. [2]With commendation.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the Royal College of Surgeons of Edinburgh held on December 19, 1951, with Professor Walter Mercer, President, in the chair, the following candidates who had passed the requisite examinations were admitted Fellows: T. L. Barclay, F. Bauer, Lydia Colaco, J. K. Craig, H. A. F. Dudley, A. S. Lambert, D. G. Lane, F. D. Martinson, S. Mishra, A. H. McCallum, J. A. McCredie, I. G. Mackenzie, S. Nand, W. H. Rutherford, L. Stein, D. P. Viljoen, J. A. S. Wilson.

Professor Robert Humphrey McKeag, M.B., B.Ch., B.Dent.Sc., of the Department of Dental Surgery, University of Ceylon, was elected a Fellow in Dental Surgery without examination.

The Services

A *Supplement* to the *London Gazette* has announced the following awards:

First, Second, and Third Clasps to the Territorial Efficiency Decoration.—Major H. R. Paterson, T.D., R.A.M.C.

First Clasp to the Territorial Efficiency Decoration.—Lieutenant-Colonel D. W. E. Lloyd, M.C., T.D., and Major H. Dickie, T.D., R.A.M.C.

Territorial Efficiency Decoration and First Clasp.—Majors G. W. Monro and J. R. S. Third, Captain J. P. Collinson, R.A.M.C.

Territorial Efficiency Decoration.—Lieutenant-Colonel E. F. Hill, Captain (Honorary Major) G. G. Cochrane, and Captain J. L. Carmichael, R.A.M.C.

CASUALTIES IN THE MEDICAL SERVICES

Prisoners of War.—Captains R. P. Hickey and D. R. Patchett, R.A.M.C., attached R.U.R.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 22** (No. 51) and corresponding week 1950.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 126 great towns in England and Wales (London included), London administrative county, the 16 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 13 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1951					1950				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	54	5	11	1	1	46	2	13	1	5
Dysentery	422	29	148	3	1	1,024	60	148	4	
Encephalitis, acute	1	0	0	0		6	1	0	0	
Enteric fever:										
Typhoid	6	0	0	0	1	5	1	0	0	2
Paratyphoid	17	0	5(B)	5	1(B)	3	0	0	1	
Food-poisoning	182	10		1		169	15		1	
Infective enteritis or diarrhoea under 2 years				16	14				11	9
Measles*	2,321	28	134	159	85	14,328	1556	197	79	120
Meningococcal infection	30	2	12	1	4	31	3	18	0	1
Ophthalmia neonatorum	27	1	10	0		37	1	9	1	
Pneumonia†	681	57	238	3	1	647	42	313	2	
Poliomyelitis, acute:										
Paralytic	22	0	9	2	0	53	6	4	0	3
Non-paralytic	6	1								
Puerperal fever§	203	22	12	1	2	74	10	6	1	
Scarlet fever	1,552	112	292	21	44	1,106	87	176	42	57
Tuberculosis:										
Respiratory			126	27				135	12	
Non-respiratory			31	10				29	12	
Whooping-cough	1,819	63	262	74	86	3,735	360	604	30	77

DEATHS in Great Towns	1951					1950				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery		0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	21		2	0	2	22		7	0	0
Influenza	13	3	0	1	0	54	4	5	1	0
Measles		0	1	0	1		1	0	0	2
Meningococcal infection		0	0				1	1		
Pneumonia	273	55		11	9	350	69		12	12
Poliomyelitis, acute	2	0			0	3	1			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	139	26	17	3	7	197	31	29	6	13
Non-respiratory		1	3	0	3		2	4	1	0
Whooping-cough	1	0	0	0	0	13	2	0	0	0
Deaths 0–1 year	257	29	31	15	22	299	39	42	10	7
Deaths (excluding stillbirths)	5,685	951	660	135	183	6,971	1085	791	154	188
LIVE BIRTHS	6,405	1050	787	267	320	6,411	995	809	206	347
STILLBIRTHS	192	37	17			164	28	21		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

London's Health in 1951

According to a preliminary report issued by Sir Allen Daley, London County Medical Officer of Health, the provisional birth rate in London for 1951 was 15.8 per thousand population. It has declined progressively from the peak of 1947, when it was 20.9. The average for the decade 1931–40 was 13.8. The provisional death rate was 12.7 per thousand, which is slightly higher than the rate for any of the years 1946–50 but the same as the rate for the decade 1931–40. This slight rise in mortality may be partly attributed to the influenza epidemic earlier in the year.

The provisional infant mortality rate was 26 per thousand live births. This was the same as the rate in 1950 and lower than any previously recorded rate. For 1931–40 the rate was 60. The provisional neonatal mortality rate (i.e., of children under four weeks) was 17.4 per thousand live births, as compared with 24 for 1931–40.

The provisional death rate for tuberculosis was 0.38 per thousand—a new low record, and 0.02 below the rate for 1950. Notifications of new cases fell slightly from 5,718 in 1950 to 5,476. Fatal road accidents increased in number; there were 303 deaths (provisional figure) as compared with 245 in 1950. There were 44 deaths from infantile diarrhoea, which is a record low figure.

Week Ending December 29

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,095, whooping-cough 1,402, diphtheria 43, measles 2,331, acute pneumonia 678, acute poliomyelitis 20, dysentery 293, paratyphoid fever 7, and typhoid fever 3.

Infectious Diseases

In England and Wales during the week ending December 22, 1951, notifications of whooping-cough decreased by 110 and measles by 127, while notifications of acute pneumonia decreased by 98 and dysentery by 85.

The decline in the incidence of whooping-cough was mainly contributed by the midland counties. The largest fluctuation was a rise of 47 in Yorkshire West Riding. Small fluctuations occurred in the local trends of scarlet fever, and the total for the country was only 9 more than in the preceding week. For the second consecutive week a rise of 12 in the number of notifications of diphtheria was recorded, and the total was the largest for over a year. The largest variations in the local trends of diphtheria were a rise of 8 in Staffordshire and a fall of 4 in Cheshire. The largest increases in the incidence of measles were Cardiganshire 71 and Kent 44, and the largest decreases were Staffordshire 61 and Durham 49.

In Suffolk 14 further cases of paratyphoid fever were notified; 10 cases were reported in this county in the preceding week. The largest centres of infection during the week were Stowmarket U.D. 8 and Hartismere R.D. 5.

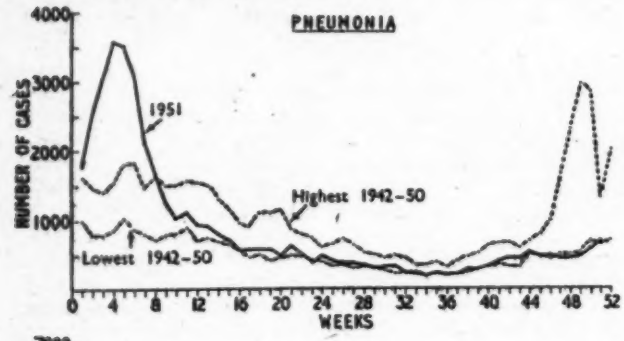
The notifications of acute poliomyelitis were 14 fewer for paralytic and 2 fewer for non-paralytic cases than in the preceding week. The largest returns during the week were those of Kent and Cambridge with 3 cases each.

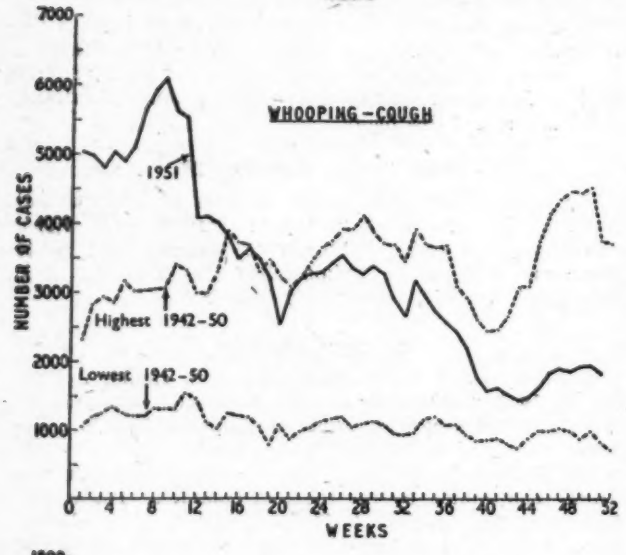
A further 93 cases of dysentery were notified during the week from the outbreak in Norwich C.B. The other large centres of infection were Middlesex 65 (Staines U.D. 13, Willesden M.B. 12); Northumberland 39 (Rothbury R.D. 37); Southampton county 31 (Portsmouth C.B. 15, Havant and Waterloo U.D. 10); London 29; Lancashire 29; Durham 17 (Jarrow M.B. 11); Essex 15; Leicestershire 12 (Leicester C.B. 12); and Yorkshire West Riding 12.

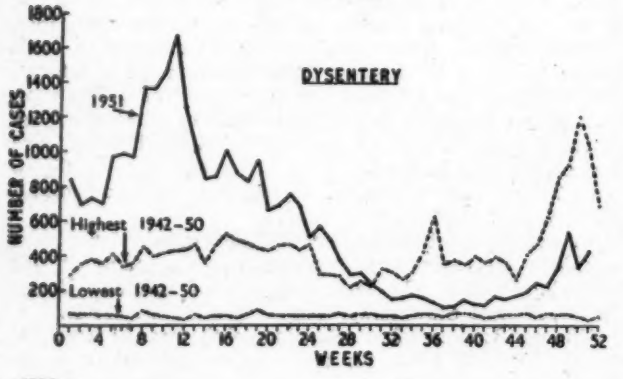
In Scotland the number of notifications of dysentery was 109 more than in the preceding week because of an outbreak in Lanark county with 101 notifications. The other large return from Scotland was 27 for Glasgow.

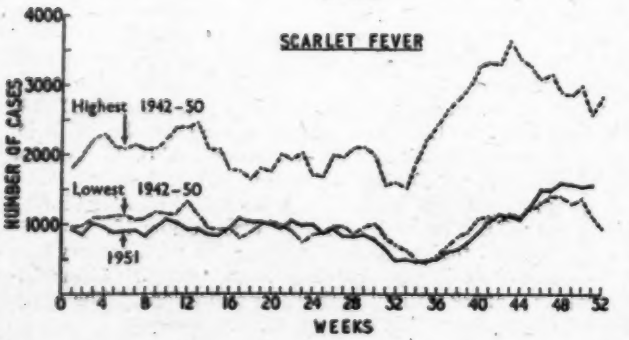
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Health in Singapore

A notable feature of the population on Singapore Island is its great increase in the last 30 years. From just over 400,000 in 1921 it has grown to just over a million in 1950 (*Annual Report* of the Medical Department of the Colony of Singapore, 1950). From 1911 to 1931 the increase was some 83%, and the cause was mainly immigration from India and China. Since 1931 the population has grown by about 82%, mainly because of the steady increase of births over deaths. While in 1931 there were 584 females to 1,000 males, there are now 855, a factor of much significance to the recent population increase.

The infant mortality rate in 1950 rose to 82 from the 1949 low record of 72. These figures may be compared with pre-war returns of 130 in 1939 and 191 in 1931; the rate in 1944 was 285. The present rate is similar to that for England and Wales in 1920. The maternal mortality rate continued to decline and was 1.85 per 1,000 total births as compared with 4.0 in 1939.

The following were the death rates per million in 1950 from certain causes (with the corresponding figures for 1939–41 in parentheses): pulmonary tuberculosis, 1,193 (2,288); malaria and unspecified fever, 806 (1,547); beriberi, 242 (873); violence, 486 (637); heart diseases, 558 (655).

Medical News

Lady Tata Memorial Trust

The Trustees of the Lady Tata Memorial Fund invite applications for grants, scholarships, or fellowships for research on diseases of the blood, with special reference to leukaemia, in the academic year beginning October 1, 1952. They are open to workers of any nationality, in any country in which payment is possible. Grants are made for research expenses or to provide scientific or technical assistants for senior workers. Scholarships are awarded for the personal support of those carrying out approved research under suitable direction; their normal value will be £600 for whole-time work, with a proportional adjustment for work on a part-time basis. In addition the Trustees may award one or more Lady Tata Memorial Research Fellowships to workers with considerable research experience; the stipend of these fellowships is £1,000 per annum. Further particulars and forms of application may be obtained by writing to the secretary of the Scientific Advisory Committee, c/o Medical Research Council, 38, Old Queen Street, Westminster, London, S.W.1. Applications must be submitted before March 31, and the awards will be announced by the Trustees in June.

Emergency Bed Service: Applications and Admissions

During the seven days ending January 7 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,294, of whom 85.23% were admitted.

Formation of a Persian Gulf Medical Society

A medical congress was held in Bahrain Island in the Persian Gulf on November 14 and 15 last. The meeting was arranged by the Bahrain Medical Society, which had invited medical organizations in the area to send representatives. Forty-five doctors attended, of whom 27 were visitors from other parts of the Persian Gulf area and beyond. Among those present were representatives of the medical departments of local governments, oil companies, and American missions, as well as medical officers from the Royal Navy and Royal Air Force. They included American, Arabian, British, Indian, Lebanese, Pakistan, and Palestinian nationalities. The congress was opened in person by the Ruler of Bahrain. The meeting was mainly clinical, and included

"Midwifery among the Arabs," by Dr. Isabel Doeg (Bahrain), "Intramedullary Nailing of Fractures," by Dr. Harold Lohnaas (Arabia), "Treatment of Juvenile Tuberculosis with Streptomycin," by Dr. Naif Hassan (Kuwait), and "National Health Service," by Dr. C. A. Bozman (Cairo). Films lent by the British Council were shown. A proposal to found a Persian Gulf Medical Society open to all bona-fide medical practitioners in the area was adopted with enthusiasm, and the second afternoon of the meeting was devoted to a discussion on its formation and constitution. In the absence of Dr. R. Biggar (Bahrain), from whom the proposal originated, Dr. W. J. Moody (Bahrain) outlined the proposed aims and scope of the society, which were (i) to bring into professional and social contact all recognized medical practitioners in the Persian Gulf area irrespective of creed or nationality, (ii) to hold an annual clinical meeting at which medical problems common to the area would be discussed, and (iii) to organize investigations in certain fields (e.g., tuberculosis, venereal disease, trachoma) of particular local interest or importance. Visitors, many of whom were accompanied by their wives, were given hospitality by the Bahrain Government, the Bahrain Petroleum Company, and various private individuals. Members of the congress and their ladies attended a dinner given by the Ruler, and were also entertained by the Political Resident and by the General Manager of the Bahrain Petroleum Company. It is hoped that the first of the annual meetings of the Persian Gulf Medical Society as such will be held in Kuwait towards the end of 1952.

Publications Received

South-east and the South-west Metropolitan Hospital Regions Maps.

North-east and the North-west Metropolitan Hospital Regions Maps; prepared by the King Edward's Hospital Fund for London, price 21s. post free.

British Journal of Psychiatric Social Work, No. 5: Association of Psychiatric Social Workers, price 5s.

M.B.E. Awarded to Laboratory Technician

Among the New Year Honours was an M.B.E. for Mr. L. W. Collison, technical officer at the National Institute for Medical Research, who is known and respected by physiologists and pharmacologists all over the world for his work as senior technical assistant in the physiological laboratories there. He started his career as a boy of 14 in the Burroughs Wellcome laboratory under Sir Henry Dale and accompanied him to the National Institute in 1920. He has designed and built apparatus for many distinguished scientists. His award is not only a recognition of his personal qualities but a sign of increasing awareness of the importance of the laboratory technician in medical research.

Australasian Annals of Medicine

The Royal Australasian College of Physicians is to publish a new journal, *Australasian Annals of Medicine.* This journal is intended for original observations and investigations. It will appear twice a year, commencing in May, 1952, and will replace the *Proceedings of the Royal Australasian College of Physicians.*

Dangerous Drugs Act, 1951

This new Act came into force on January 1, and consolidates all existing legislation in this field without introducing any novelties. It is therefore now the sole legal reference.

Wills

Mrs. Evelyn Imelda Chichester Tudor-Edwards, widow of Mr. A. Tudor-Edwards, left £92,014. She left £5,000 to the President and Council of the Royal College of Surgeons of England, to found a Fellowship for the advancement of and research into surgical science.

COMING EVENTS

Oxford Medical Club Dinner

The Oxford Graduates Medical Club dinner is to be held at the Royal College of Surgeons on February 8. Tickets (30s.) can be obtained from the honorary secretary, 73, Harley Street, London, W.1.

Religion and Evolution

A conference on religion and evolution will be held at University College, London, on March 7 and 8. Ample time will be allowed for discussion of the interrelations between religion and evolution, and particularly of the practical problems encountered by teachers in the classroom. The fee for the whole conference is 7s. 6d., and for single sessions 2s. 6d. Tickets may be obtained from the Secretary, British Social Biology Council, Tavistock House South, Tavistock Square, London, W.C.1.

First European Congress of Cardiology

A European congress of cardiology will be held in London in September, 1952, organized by the British Cardiac Society, which has appointed Sir John Parkinson to act as chairman of the congress, in collaboration with the presidents of the European Society of Cardiology. The congress will be open to all members of European national cardiac societies affiliated to the European Society of Cardiology, and will be limited to them. Non-members may attend the scientific sessions by invitation of the organizing committee. The congress will be held at the University of London, Bloomsbury, W.C. The Chancellor's Hall at the University will open at 10 a.m. on Tuesday, September 9, for registration and for distribution of papers, tickets, and information. The scientific sessions will be held on September 10, 11, and 12 in the Beveridge Hall and the Deller Hall in the University building. Forms of application for membership will be sent out soon and further details of the programme will be announced. All correspondence relating to the congress should be addressed to Dr. K. Shirley Smith, Organizing Secretary, the European Congress of Cardiology, the Institute of Cardiology, 35, Wimpole Street, London, W.1.

International Diabetes Federation Congress

A congress on diabetes mellitus will be held at Leyden, Netherlands, from July 7 to 12, 1952. Further details may be obtained from Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

International Society of Haematology

The fourth international congress will be held in Mar del Plata, Argentina, September 21 to 26. Subjects to be discussed include the aetiology and treatment of leukaemias, polycythaemia of altitude, haemolytic disease in newborn infants, etc. The registration fee has been fixed at $100 (Argentine currency), and all information may be obtained from the secretaries-general, Dr. Marcel Bessis, 53, Boul. Diderot, Paris, 12e, and Dr. Sol Haberman, 3301, Junius Street, Dallas, Texas, U.S.A.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday

●INSTITUTE OF DISEASES OF THE CHEST AND INSTITUTE OF CARDIOLOGY.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 11, 5.30 p.m., "*Surgery of the Heart: General Survey,*" by Dr. Maurice Campbell.

WEST KENT MEDICO-CHIRURGICAL SOCIETY.—At the Miller Hospital, Greenwich High Road, London, S.E., January 11, 8.30 p.m., The Purvis Oration by Sir Heneage Ogilvie.

Monday

HUNTERIAN SOCIETY.—At Mansion House, London, E.C., January 14, 8.30 p.m., "*Endocarditis*," Hunterian Lecture by Professor W. Löffler (Zurich).

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—January 14, 5.30 p.m., lecture-demonstration for postgraduates by Dr. E. Stengel.

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—January 14, 8.30 p.m., "*Radioactive Isotopes*," discussion to be introduced by Professor E. J. Wayne and Mr. H. Miller.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—January 14, 5 p.m., "*Non-paralytic Strabismus. The Care and Treatment of the Squinting Child*," by Dr. T. H. Whittington.

Tuesday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 15, 5.30 p.m., "*The Philosophy of Science*," by Professor H. Dingle, D.Sc.

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 41, Queensgate Terrace, London, S.W., January 15, 8.30 p.m., fourth ordinary meeting of 55th session. "*Mount Everest*," discussion to be opened by Dr. Raymond Greene. Illustrated with lantern slides.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 15, 5.30 p.m., "*Skin Manifestations of Malignant Diseases*," by Dr. L. Forman.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—January 15, 5 p.m., "*Some Concepts of Rheumatic Disease*." Goulstonian Lecture by Dr. J. H. Kellgren. (See also January 17.)

Wednesday

BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles Street, Birmingham.—January 16, 8 p.m., inaugural meeting of new Section of Psychiatry of Birmingham Medical Institute.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 16, 5.30 p.m., "*Mycology—Actinomycosis and Nocardiosis*," by Dr. R. W. Riddell.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., January 16, 4.30 for 5 p.m., "*Retention of Urine in Childhood*," by Mr. D. I. Williams.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—January 16, 5 p.m., "*Misnomers in Tumour Nomenclature*," Finlayson Memorial Lecture by Professor R. A. Willis.

ROYAL MICROSCOPICAL SOCIETY, Tavistock House South, Tavistock Square, London, W.C.—January 16, 5.30 p.m., annual general meeting. Film demonstration: "*Motility and Flagella*," by Professor A. Pijper; "*Instrumental Insemination of Bees*," by Mr. C. P. Abbott, in collaboration with Rothamsted Experimental Station; "*Life Cycle of the Malaria Parasite*," by Research Laboratories, I.C.I., Ltd.

Thursday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—January 17, 8 p.m., "*The Radiological Diagnosis of Intracranial Tumours in Children*," by Dr. J. W. D. Bull.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 17, 5.30 p.m., "*Fundamentals of Cortical Physiology*," by Sir Geoffrey Jefferson, F.R.S.

EDINBURGH CLINICAL CLUB.—At B.M.A. Rooms, 7, Drumsheugh Gardens, Edinburgh, January 17, 8 p.m., "*The Treatment of the Menopause*," by Dr. T. N. MacGregor.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool.—January 17, 8 p.m., ordinary meeting. "*Our Heritage—the Origin and Development of the Liverpool Medical Institution*," by Mr. W. A. Lee.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 11, Chandos Street, W., January 17, 8.30 p.m., "*The Nutritional Assessment of the Individual*," address by Professor John Yudkin.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—January 17, 5 p.m., "*Some Concepts of Rheumatic Disease*," Goulstonian Lecture by Dr. J. H. Kellgren. (See also January 15.)

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—January 17, 5 p.m., "*Corneal Infections and their Specific Treatment*," ophthalmology lecture by Professor Arnold Sorsby.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26, Portland Place, London, W., January 17, 7.30 p.m., ordinary meeting. "*The Treatment of Leprosy with D.D.S.*," by Dr. Ernest Muir; "*The Action of Sulphones in Leprosy, with Particular Reference to Histopathology*," by Dr. R. G. Cochrane. A discussion will follow.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, January 17, 5 p.m., "*The Application of the Electron Microscope to Bacteriology*," by Dr. J. E. McCartney, D.Sc.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—January 17, 4.30 p.m., lecture-demonstration in psychiatry by Sir Paul Mallinson.

UNIVERSITY COLLEGE, Anatomy Theatre, Gower Street, London, W.C.—January 17, 1.15 p.m., "*What is Pharmacology?*" by Dr. H. O. Schild.

Friday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—January 18, 5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—January 18, (1) at Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., 4 p.m., meeting of Radiotherapy Section. "*The Clinical Features and Types of Intracranial Tumours Found in Children*," by Professor Norman Dott; "*The Combined Roles of Surgery and Radiotherapy in the Treatment of Intracranial Tumours in Children*," by Mr. John Gillingham; "*The Pathology of Intracranial Tumours in Children*," by Dr. Martin Bodian. (2) At Royal Society of Medicine, 1, Wimpole Street, London, W., 8.15 p.m., "*The Diagnosis and Radiotherapy of Intracranial Tumours in Children*," by Mr. J. Jackson Richmond and Dr. Edith Paterson; "*The Treatment of Megaloblastoma*," film by Dr. Edith Paterson.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 18, 5.30 p.m., "*Medical Writing*," by Dr. W. R. Bett.

●INSTITUTE OF DISEASES OF THE CHEST AND INSTITUTE OF CARDIOLOGY.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., January 18, 5.30 p.m., "*Surgery of the Heart: Techniques of Investigation*," by Dr. Aubrey Leatham.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—January 18, 8 p.m., "*The Curious Effects of Carbon Monoxide Poisoning*," by Dr. James K. Slater.

Saturday

BIOCHEMICAL SOCIETY.—At Middlesex Hospital Medical School, London, W., January 19, 10.30 a.m., 304th meeting. Scientific papers will be read.

APPOINTMENTS

The King has appointed Dr. George Brewster to be Surgeon-Apothecary to the Household at Holyroodhouse Palace in succession to Dr. N. S. Carmichael, deceased.

Dr. Vernon Frederick Hall, Dean of King's College Hospital Medical School, London, S.E., has been appointed a member of the South-east Metropolitan Regional Hospital Board in succession to the late Mr. J. B. Hunter.

COUSINS, B. A., M.Sc., M.B., B.Ch., Medical Registrar, Norfolk and Norwich Hospital, East Anglian Regional Hospital Board.

CRAIG, C. McK., junior, M.B., B.S., F.R.C.S., Consultant Surgeon to Lowestoft Hospital, Norfolk and Norwich Hospital Group, East Anglian Regional Hospital Board.

DIVILLY, PATRICK JOSEPH, L.R.C.P.&S.I., L.M., Medical Officer, Feakle Dispensary District, Co. Clare, Eire.

INMAN, G. K. E., M.B., Ch.B., D.M.R.D., Senior Registrar in Radiology to Bristol Clinical Area, South-western Regional Hospital Board.

LEWIS, T. L. T., M.B., B.Chir., F.R.C.S., M.R.C.O.G., Obstetric Surgeon, Queen Charlotte's Maternity Hospital, Goldhawk Road, Hammersmith, London, W.

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Senior Resident Medical Officer at New Hall Hospital, Southport*, R. S. Cook, M.B., Ch.B. *Whole-time Assistant Radiologist to Hospitals in St. Helens and Warrington Areas*, A. Attwood, M.B., B.Ch., D.M.R.D. *Part-time Consultant Dermatologist to Clatterbridge General Hospital*, D. G. Freshwater, M.B., B.Chir., M.R.C.P. *Consultant Physician to Clatterbridge General Hospital*, M. W. W. Wood, M.D., M.R.C.P.

MACLACHLAN, JAMES, M.B., Ch.B., D.P.H., Medical Officer of Health and Port Medical Officer, County Borough of Barrow-in-Furness, and School Medical Officer.

MANCHESTER REGIONAL HOSPITAL BOARD.—*Consultant General Physicians, Crumpsall Hospital, Manchester*, M. D. Milne, M.D., M.R.C.P., R. V. Dent, M.B., B.Chir., M.R.C.P. *Consultant Obstetrician/Gynaecologist, Withington Hospital, Manchester*, R. W. Burslem, M.D., M.R.C.O.G.

MOORE, ROBERT, M.B., B.S., M.R.C.P., Senior Medical Registrar, St. Andrew's Hospital, Devons Road, London, E.

ROUTLEDGE, R. T., M.B., B.S., F.R.C.S., Senior Registrar in Plastic Surgery, Bristol Clinical Area, South-western Regional Hospital Board.

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Consultant (Assistant) Obstetrician and Gynaecologist, Portsmouth Group of Hospitals*, J. J. Foley, M.B., B.Ch., M.R.C.O.G. *Whole-time Consultant Physician, Portsmouth Group of Hospitals*, E. H. Minors, M.B., Ch.B., M.R.C.P., D.C.H. *Part-time Consultant Physician, Chelsea Group of Hospitals*, R. Daley, M.D., M.R.C.P. *Part-time Consultant Physician for Chest Diseases, Chelsea Group of Hospitals*, L. J. Grant, M.B., B.S., M.R.C.P. *Whole-time Physician-Superintendent and Consultant Psychiatrist, Netherne Hospital*, R. K. Freudenburg, M.D., D.P.M. *Whole-time Consultant Child Psychiatrist, Hampshire Child Guidance Service*, Daisy G. Iliff, M.R.C.S., L.R.C.P., D.P.M. *Whole-time Consultant Anaesthetist, Woking and Chertsey Group of Hospitals*, Eileen McC. Gibson, M.B., B.Ch., D.A. *Part-time Consultant Anaesthetist, Isle of Wight Group of Hospitals*, R. T. V. Clarke, B.M., B.Ch., D.A. *Part-time Consultant Ophthalmologist, Fulham and Kensington Group of Hospitals*, P. Ll. Blaxter, M.B., B.Chir., F.R.C.S., D.O.M.S. *Part-time Assistant Thoracic Surgeon, Godalming, Milford, and Liphook Group of Sanatoria*, C. E. Drew, M.B., B.S., F.R.C.S. *Part-time Consultant Surgeon, Woking and Chertsey Group of Hospitals*, M. T. Pheils, M.B., B.Chir., F.R.C.S.

Part-time Consultant Radiologist, Woking and Chertsey Group of Hospitals, R. O. Murray, M.B., B.Chir., D.M.R. *Whole-time Assistant Chest Physician (S.H.M.O. Grade), Dorset and Poole Areas*, A. E. K. Salvi, M.R.C.S., L.R.C.P. *Whole-time Assistant Chest Physician (S.H.M.O. Grade), Southampton Area*, Mary F. Brownlie, M.B., Ch.B., D.P.H. *Consultant Chest Physician, Southampton Area*, W. M. MacLeod, M.B., B.S., M.R.C.P. *Registrar (Orthopaedic Surgery), Croydon Group of Hospitals*, G. M. Bedbrook, M.B., B.S., F.R.C.S., F.R.A.C.S. *Registrar (Anaesthetics), Salisbury General Hospital*, V. P. Wordsworth, M.R.C.S., L.R.C.P. *Registrar (Anaesthetics), St. Luke's Hospital, Guildford*, Kathleen J. Logan, M.B., Ch.B. *Registrar (Obstetrics and Gynaecology), Nelson Hospital*, I. M. G. Mackay, M.R.C.S., L.R.C.P., D.Obst.R.C.O.G. *Registrar (Infectious Diseases), Western Hospital*, S. Y. To, M.B., B.S., D.T.M.&H. *Registrar (Medical Department), Milford Chest Hospital*, Eudora M. R. Davies, M.B., Ch.B. *Senior Registrar (Psychiatrics), Brookwood Hospital*, E. R. F. Mellon, M.B., B.Ch., D.P.M., D.P.H. *Registrar (Psychiatrics), West Park Hospital*, R. D. Watson, M.B., B.S. *Registrar (Psychiatrics), Cassel Hospital*, W. A. Saffery, M.B., B.Ch.

WILLIAMS, D. LLOYD, L.R.C.P.&S.Ed., L.R.F.P.S.(Glasg.), Assistant Medical Officer of Health and Assistant School Medical Officer for the County of Merioneth.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Harris-Jones.—On December 23, 1951, at Sheffield, to Carol (formerly Mackenzie), wife of J. N. Harris-Jones, M.D., M.R.C.P., a sister for Richard (George).

Marrian.—On December 31, 1951, at Cambridge, to Biddy Kingsley Pillers, M.B., B.Chir., wife of Denis H. Marrian, a son.

Mathers.—On December 22, 1951, at the Military Hospital, Malta, to Diana (formerly Mould), wife of Dr. George C. Mathers, a son.

Thomas.—On December 28, 1951, at the Maternity Hospital, Royal Infirmary, Preston, to Morfudd (formerly Humphreys), M.B., Ch.B., wife of Dr. William M. Thomas, a second daughter.

Wilson.—On January 2, 1952, at the South London Hospital for Women, to Agnes Christian (formerly Gillan), O.B.E., M.B., Ch.B., wife of William Proctor Wilson, C.B.E., B.Sc., M.I.E.E., a son.

DEATHS

Adam.—On December 26, 1951, at 10, Russell Place, Edinburgh, James Robertson Adam, M.B., Ch.B., D.P.H.

Aldous.—On January 3, 1952, Herbert James Aldous, L.S.A., L.R.C.S.Ed., of Boundary Stone, Pauisgrove, Portsmouth, Hants, aged 76.

Anderson.—On December 26, 1951, at 70, Wadsley Lane, Sheffield, Alexander Anderson, M.B., C.M., D.P.H., aged 84.

Benson.—On December 28, 1951, in Somerset, Wallace Benson, C.B.E., D.S.O., M.B., B.Ch., Colonel, A.M.S., retired.

Bulleid.—On December 27, 1951, at his home, Dymboro, Midsomer Norton, Somerset, Arthur Bulleid, L.R.C.P.&S.Ed., L.R.F.P.S., aged 89.

Carr.—On December 30, 1951, at Woodhouse, Windsor Road, Gerrard's Cross, Bucks, Mona Carr (formerly Kirkhouse), M.D.

Cock.—On December 29, 1951, at his home, 7, Gipsy Hill, Upper Norwood, London, S.E., Gerald Cock, M.R.C.S., L.R.C.P.

Davies.—On December 28, 1951, at his home, 2, Morfa Lane, Carmarthen, Arthur Lewis Davies, M.R.C.S., L.R.C.P.

Dickenson.—On January 6, 1952, at Newsbott, Haslemere, Surrey, George Oswald Morrell Dickenson, M.B., B.S., Surgeon Captain, R.N., retired.

Ferguson.—On December 29, 1951, at St. Andrews, Joshua Ferguson, M.B., C.M., F.R.F.P.S., of 11, Windmill Road, St. Andrews, Fife, aged 80.

Geraghty.—On January 3, 1952, at the Manchester Royal Infirmary, William Geraghty, M.B., Ch.B., of "Glenesk," Ashton Lane, Sale, Cheshire, aged 54.

Jackson.—On December 28, 1951, at Plas Uchaf, Penmaenmawr, Caernarvonshire, Robert Jackson, T.D., M.B., C.M., Colonel, A.M.S., T.A., retired, aged 89.

Jameson.—On December 26, 1951, at Queen Victoria Hospital, East Grinstead, Surrey, George Dearden Jameson, M.R.C.S., L.R.C.P., D.P.H., Lieutenant-Colonel, R.A.M.C., retired, of Chilling Street Cottage, Sharpthorne, Sussex.

Kohn.—On December 15, 1951, at 62, Alexandra Road, Wimbledon, London, S.W., Elizabeth Kohn, M.B., B.S., M.R.C.P.Ed., late of Rangoon, Burma.

Lys.—On December 29, 1951, at Emo Lodge, Bournemouth, Henry Grabham Lys, M.D., M.R.C.P., aged 87.

MacGibbon.—On January 3, 1952, at 30, New North Road, Huddersfield, Robert Robertson MacGibbon, L.R.C.P.&S.Ed., L.R.F.P.S., aged 52.

Mailer.—On January 2, 1952, at 5, South Close, Highgate, London, N., William Mailer, M.B., C.M.

Malone-Barrett.—On December 26, 1951, at Aveland, East Dean, Eastbourne, Sussex, Francis Malone-Barrett, M.B., B.Ch.

Miller.—On January 1, 1952, at a nursing-home, Edinburgh, Ada Elizabeth Miller, M.D., D.P.H., of 6, Cobden Road, Edinburgh.

Miller.—On December 31, 1951, William Henry Miller, M.D., F.R.C.S., of 43, St. Peters Street, Bedford, aged 70.

Nix.—On December 31, 1951, at Chatteris, Cambs, Rupert Edward Nix, M.B., B.Ch., J.P., aged 84.

Peace.—On January 1, 1952, at Tellisford, Burry Port, Carmarthen, Percy Clift Peace, M.R.C.S., L.R.C.P.

Peake.—On January 4, 1952, at his home, "Keeps," Hillside, Horsham, Sussex, William Pemberton Peake, T.D., M.R.C.S., L.R.C.P.

Richmond.—On December 16, 1951, Henry Richmond, M.B., Ch.B., D.P.H., of 314, Wigan Road, Standish, Wigan, Lancs, aged 64.

Robbins.—On December 25, 1951, in London, Frank Hubert Robbins, M.C., M.B., F.R.C.S.Ed., aged 64.

Skeels.—On January 5, 1952, in London, Percy Bernard Skeels, L.M.S.S.A.

Smith.—On December 26, 1951, at Stronsay, Whickham, Co. Durham, Edward Davison Smith, M.B., B.S., aged 67.

Smyth.—On December 26, 1951, at Buxton, Richard Smyth, M.D., M.Ch., formerly of Ningpo, China, aged 88.

Willson.—On January 4, 1952, Reginald John Willson, M.B., B.Ch., D.P.H., of Newlands, Carlton Road, Redhill, Surrey, aged 77.

Wilson.—On December 29, 1951, at Finchley, London, N., Helen Mary Wilson, M.D., J.P., formerly of Sheffield, aged 87.

Wyllie.—On December 27, 1951, at 10, York Gate, London, N.W., Hugh Alexander Wyllie, M.B., B.S.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

How to Test Schoolchildren's Hearing

Q.—*What tests for hearing are recommended for the routine medical inspection of schoolchildren? What result with each would you consider an indication that the child required treatment for deafness?*

A.—An ideal test for this purpose involves the use of a gramophone audiometer which replays over headphones a randomized list of single digits or simple words at intensities decreasing in about 3-decibel steps. Up to 40 children may be tested simultaneously by this means. An average hearing loss of 10 decibels in one or both ears should be considered as an indication of requirement of further investigation. Another test, which is very satisfactory, is known as the "sweep frequency test." This consists in setting the output intensity of a pure-tone audiometer at a very quiet level—say that corresponding to a hearing loss of 10 decibels—and seeing if the child responds to the various tones at this level. Failure to respond to two or more tones can be considered as indicating further investigation.

A less efficient but, for reasons of economy, frequently chosen method is the measurement of the maximum distance at which each ear can hear forcibly whispered numbers or simple syllables, the untested ear being closed with a finger and turned away from the examiner. The child is asked to repeat the words heard, and if the maximum distance for 90% success is 20 ft. (6 metres) or more the ear under test may be regarded as normal. Particular attention should be given to the child's hearing for consonants. It must be remembered that the presence of background noise in the test-room will raise the threshold of hearing by an amount dependent on the level of the disturbance, and this should be borne in mind in interpreting results. The acoustic properties of the test-room also contribute to the unreliability of the test.

Should one of these tests indicate subnormal hearing, the child should be further examined by an otologist, who will, if the deafness is confirmed, advise upon the question of treatment.

Any information such as difficulty in hearing the teacher's voice in the classroom should be taken into consideration. Serious retardation of speech development may, though not always, be an indication of some degree of hearing loss, particularly to high frequencies.

Thumb-sucking

Q.—*Where can I find information on the management of a child who sucks his thumb?*

A.—On p. 194 of the book "*Any Questions?*" The book can be obtained for 7s. 6d. (postage 6d.) from the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

Discoid Lupus Erythematosus

Q.—*What is the best treatment for discoid lupus erythematosus of the scalp in an elderly woman? What is the prognosis?*

A.—The cause of discoid lupus erythematosus is unknown and there is no specific therapy. The condition may be influenced by any other organic or functional state which may be present, and this should receive attention. If there is no contraindication, gold therapy is valuable and may cure or arrest progress of the disease. Mepacrine in a dose

of 100 mg. twice a day was more effective than other measures in a series of cases recently reported.

The prognosis is bad in the sense that the condition destroys skin and hair and produces an irreversible, scarring alopecia. The disease does not affect the general health. If extensive, ulceration sometimes occurs, which generally responds to small doses of sulphonamide by mouth and locally, but this treatment must be used with care. Malignant changes are rarely seen.

Prognosis in Retinitis Pigmentosa

Q.—*What is the outlook for a boy of 10 who has retinitis pigmentosa (diagnosed by two eye specialists)? Difficulty of vision, only in the dark, was first noticed six years ago after an attack of kala azar treated by antimony. The parents have been told that the child will eventually become blind. How quickly will this happen?*

A.—The development of nightblindness in retinitis pigmentosa as early as the age of 4 is unusual; so also is a diagnostic fundus appearance at the age of 10. This in itself raises doubt whether one is dealing with the classical form of hereditary retinitis pigmentosa, though such early changes may occur in the severe, but rare, sex-linked type. A full family history is needed, and also information on whether the boy shows the characteristic field defects of retinitis pigmentosa. If the boy is actually suffering from genetically determined retinitis pigmentosa there is no treatment, and it is impossible to indicate how rapidly his vision will deteriorate. If his affection is of the sex-linked type, serious trouble is almost certain by the age of 25 years.

The history of kala azar treated by antimony may be significant. With the unusual findings in this case it is possible that the nightblindness and pigmentary changes were precipitated by either the infection or the treatment. The picture of retinitis pigmentosa has been observed in measles, after vaccination, and after quinine treatment of malaria. In these cases the tendency is for some improvement rather than deterioration.

Angina and Cold Weather

Q.—*A woman of 56, who has angina, has an opportunity to go to Ontario, where the winter climate is cold and dry. Will this be likely to precipitate her anginal attacks, which are often brought on here by cold nights?*

A.—Although Sir Thomas Lewis was unable to demonstrate that cold played any part in precipitating attacks of angina pectoris, general experience has shown that it does. There is no doubt that cold may raise the blood pressure in susceptible individuals, and this may help to provoke an attack by increasing the work of the heart. In the particular case in question it seems clear that cold is harmful, and the patient would surely be unwise to go to Ontario.

Cytochrome c and Carbon Monoxide Poisoning

Q.—*What are the functions of cytochrome c? It has been suggested that it might be a useful analeptic for cases of carbon monoxide poisoning after mining accidents. Is there a sound basis for this view?*

A.—Cytochrome *c* is a respiratory catalyst which is required for the utilization of the oxygen reaching the tissues from the blood. In carbon monoxide poisoning, less oxygen reaches the tissues because some of the haemoglobin, the respiratory carrier in the blood, is combined with carbon monoxide. The question is probably inspired by a report that cytochrome *c* is beneficial in conditions of anoxia. Exhaustive trials in many laboratories have failed to confirm this report. In any case, even if cytochrome *c* could increase the rate of utilization by the tissues of the limited amount of oxygen reaching them in carbon monoxide poisoning, this would probably be more harmful than useful, since the oxygen would be depleted more rapidly. Cytochrome *c* does not combine with carbon monoxide, so it is useless as a direct antidote.

Camphorated Oil

Q.—*Am I right in believing that rubbing the chest with olive oil or camphorated oil, or any other preparation, serves no useful purpose and may even be harmful in the treatment of an infant or child suffering from bronchitis?*

A.—Unless the rubbing is over-vigorous or prolonged or the preparation too strong, in which case dermatitis may follow, no harm is likely to result from the use of a medicated oil in cases of bronchitis. On the other hand, no great therapeutic response can be expected; the counter-irritation may be of some slight value, and in the case of an oil or ointment containing menthol or camphor some inhalation of vapour will follow, and this may be helpful in clearing the upper air-passages.

Pills for Bankrupt Smokers

Q.—*I have tried to purchase locally from many chemists some pills which are sold for the prevention of smoking, but I have been unable to buy them or find a formula for their preparation. The pills I have in mind are normally dissolved in the mouth, and, while being quite tasteless themselves, produce a very nasty taste if the subject tries to smoke a cigarette. I would be grateful if you could tell me their formula.*

A.—The formula of the pills is as follows: dried sulphate of iron, 67.85%; potash alum, 17.85%; lactose, 14.28%; acacia, 0.75%; green colouring matter and excipient, q.s. They should be kept out of the reach of children.

Speedy Hypnotic

Q.—*What sedative has the quickest and shortest action when taken orally?*

A.—The hypnotics with the quickest and most evanescent action are probably pentobarbitone sodium and sodium propylallylbarbiturate. There is not much to choose between them. The dose is from 1½ to 3 gr. (0.1 to 0.2 g.). They are effective within half an hour, and are certainly not active for longer than six hours.

Lymph Drainage of Nasal Sinuses

Q.—*What is the lymphatic drainage of the accessory air sinuses? I have been unable to find information about this in standard anatomical and surgical textbooks.*

A.—The best account may be found in *Histopathology of the Ear, Nose and Throat* by Eggston and Wolff (Williams and Wilkins, Baltimore, 1947). Quoting papers by J. M. Robison (*Tex. J. Med.*, 1944, **40**, 193; *Arch. Otolaryng., Chicago*, 1944, **40** 385), these authors state that drainage is probably to a pretubal lymph plexus, thence to lateral retropharyngeal lymph nodes, and partly to submaxillary nodes, and so to the deep cervical chain.

NOTES AND COMMENTS

Honours List: Correction.—Mr. CHARLES E. DREW, who became M.V.O. in the New Year Honours, is a member of the consultant staff of the Westminster Hospital, having been appointed as fourth assistant surgeon on April 9, 1951. We regret that this hospital appointment was incorrectly given in last week's *Journal* (January 5, p. 44).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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